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Complete List of Authors:	Makia, Christine Masong; Catholic University of Central Africa, Social Sciences and Management Fesuh, Nono Betrand; National Advanced School of Engineering, University of Yaoundé 1, Cameroon, Department of Mathematics and Physical Sciences Tchoffo, Marlene; Catholic University of Central Africa, Social and Management Sciences Gamba, Victoria A; University of Nairobi, Department of Obstetrics and Gynecology Oluwole, Akinola Stephen; Federal University of Agriculture Abeokuta, Department of Pure and Applied Zoology Stothard, Russell; Liverpool School of Tropical Medicine, Department of Tropical Disease Biology
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Title: Urogenital Schistosomiasis (UGS) and Female Genital Schistosomiasis (FGS) in Cameroon: An in-depth assessment of reproductive health determinants of girls and women in the Matta Health Area

Authors: Makia Christine Masong[1,*], Fesuh Nono Betrand[2], Tchoffo Marlene Nstinda[1], Victoria A. Gamba[3], Akinola Stephen Oluwole[4], J. Russell Stothard[5]

[1]Department of Social Sciences and Management, Catholic University of Central Africa, Yaoundé, Cameroon

[2]Department of Mathematics and Physical Sciences, National Advanced School of Engineering, University of Yaoundé 1, Cameroon

[3]Department of Obstetrics and Gynecology, University of Nairobi, Nairobi, Kenya

[4]Department of Pure and Applied Zoology, Federal University of Agriculture, Abeokuta, Nigeria

[5]Department of Tropical Disease Biology, Liverpool School of Tropical Medicine, Liverpool, L3 5QA, UK

*Corresponding author

Makia Christine Masong

Department of Social Sciences and Management, Catholic University of Central Africa, Yaoundé, Cameroon

Projet MTN/OCEAC

masongbye@yahoo.com

Abstract

Objectives and Setting: Across sub-Saharan Africa, Urogenital Schistosomiasis (UGS), in particular Female Genital Schistosomiasis (FGS) is a significant waterborne parasitic disease. FGS affects the well-being of millions of girls and women, yet its direct burden upon sexual and reproductive health (SRH), of sufferers is infrequently measured, as is the case in Cameroon. Our study therefore focused upon FGS and sought to identify current associations with several key reproductive health indicators, to provide formative information for better integrated control with UGS.

Participants: From a population of 304 females all examined for UGS by urine filtration and microscopy (UGS prevalence = 63.8%; 95% CI: 58.3–69), an unbiased sub-group of 67 girls and women aged >13 was examined clinically for FGS. This included application of portable colposcopy, a technique not available in routine primary care, with observed sequelae classified according to the WHO FGS pocket atlas.

Outcome: Within this sub-group, the prevalence of FGS was 50.7% (34/67) and 59.7% (40/67) for UGS, with most common FGS pathologies being abnormal blood vessels, homogenous yellow sandy patches and grainy sandy patches.

Results: Epidemiological associations with FGS and UGS were investigated by univariate and multivariate logistic regression analyses. In terms of age of sufferers, FGS increased significantly with ascending age, whilst a non-significant decrease with descending age was observed for UGS. Of note, girls and women with FGS exhibited increased menstrual abnormalities/irregularities (MI). Lower abdominal pain (LAP) was identified as the only significant shared symptom of both FGS (AOR 9.5; 95% CI: 1.7-81.5) and UGS (AOR 4.3; 95% CI: 1.4-14.4), while LAP with MI appeared a strong epidemiological flag for FGS.

Conclusion : LAP and MI provide two under-explored dimensions in SRH that could be exploited in future for targetting of praziquantel provision to FGS sufferers within primary care, complementary with existing distribution for UGS sufferers.

Keywords: *Schistosoma haematobium*, clinical colposcopy, questionnaires, menstrual health, abdominal pain

Key Messages

What is already known on this topic

- Whilst millions of women in Cameroon have UGS, its epidemiological connection with FGS is not fully appreciated, which creates an unfortunate knowledge bottleneck for effective control at the public health level

What this study adds

- A detailed insight into the connection of FGS and UGS within a primary care setting, denoting those with cardinal symptomologies more explicitly for scalable detection and targeted control of FGS within UGS endemic areas

- Using clinical colposcopy combined with an analysis of sexual and reproductive health determinants, we develop a simple questionnaire approach which can better capture FGS sufferers within endemic areas for UGS

How this study might affect research, practice or policy

- Formative evidence is provided with initial recommendations, towards developing better national surveillance and control of FGS, thereby better empowering women's health within the Central African Region

Introduction

Urogenital schistosomiasis (UGS) and female genital schistosomiasis (FGS) although are both caused by infection with *Schistosoma haematobium*, a waterborne blood fluke, each appear to have rather obscure epidemiological associations, largely due to insufficient disease surveillance[1-3]. In sub-Saharan Africa where UGS is endemic and can be highly prevalent (>50%), insufficient or infrequent efforts have been undertaken to document FGS specifically, partly as the clinical skills to do so are bottlenecked within primary care[2]. While active UGS does not readily predict FGS, since FGS can occur without the direct presence of schistosome eggs in urine (a cardinal diagnostic for UGS[4]), rather FGS often presents with a more chronic time frame where schistosome eggs trapped within the cervico-vaginal surfaces[3, 5, 6]. For some, these trapped eggs can accumulate from very early on in life with enduring and typically hidden or cryptic sequelae[5, 7]. Based on several plausible biological determinants, the mucosal damage and fibrotic scarring of the vaginal and cervical surfaces from FGS proceeds with increasing duration of UGS infection(s)[3]; moreover, FGS-specific sequelae maybe slow to resolve upon standard antiparasitic treatment of UGS, i.e., single annual administration of praziquantel at 40mg/g as used in public health campaigns[3, 5].

In many parts of Africa where surveillance of UGS is poor and that for FGS is largely absent, there is a clear need to better understand the epidemiological associations between UGS and FGS. Particularly so to support earlier diagnosis of cases of FGS and individualize praziquantel treatment needs to better avert their disease progression; current interventions against UGS do not specifically target adolescent girls or women[8] though with the new WHO 2022 guideline, there is new encouragement to do so[9]. This gap in treatment coverage also has considerable bearing on progress towards elimination of schistosomiasis transmission within disease endemic communities[9].

In recent years, FGS focused research and public health education[10] has gained traction in certain countries such as Ghana and Madagascar, although other countries ,such as Cameroon currently lag behind. Schistosomiasis exists in several regions of Cameroon affecting over 10 million people in rural and urban areas[11], and the country has a national coordinated control plan for fairly early interventions during child-hood years (from 5 – 14 years old). These take advantage of school based

intervention platforms[12, 13] and in certain settings with community based interventions where their at-risk status is high[13, 14]. Over the last decade, there has been an approximate 70% reduction of schistosomiasis prevalence amongst school-aged children by 2019[11]. However, due to existing policy gaps and program intervention bottlenecks, some of the adolescent at-risk populations do not always benefit from praziquantel treatment[15] and in respect of FGS, many girls and women are missed out in treatment campaigns and not provided with adequate individualized treatments.

To address this treatment deficit, with better knowledge on the precise associations between UGS and FGS, future control policies and intervention campaigns can be revised to better target at-risk populations. For example, this could be upon future activation of integrated primary health care for better management of FGS, which is currently lacking. Understanding the risks and associations of these UGS and FGS, especially within different contexts of women's health, sheds greater light on the disease epidemiology, which could foster improved control measures both locally and nationally. Furthermore, precisely documenting existing associations between both FGS and UGS clarifies further the strong need for precision mapping of schistosomiasis in endemic regions, for formulating a better targeted integrated response.

In our study, we sought to clarify existing associations between FGS and UGS, highlighting cardinal symptomologies for scalable detection and targeted control of FGS within UGS endemic areas. This supports the need for a future integrated approach for control of schistosomiasis, and limits the "gap" concerning FGS surveillance within current primary care.

Materials and Methods

Ethics approval and consent to participate

Ethical clearance for the study was provided by the Cameroon National Ethics committee on Human Health Research (Ref N ° 2020/07/1266/CE/CNERSH/SP), with administrative authorizations from both from the Regional Delegation of Public Health for the West region of Cameroon (Ref N° 679/L/MINSANTE/SG/DRSPO/CBF), the district Health Office of the Malanteoun Health District (Ref N° 078/L/MINSANTE/DRSPO/DSMLT). Informed written and oral consent was obtained from

all participants for parasitological and gynecological examinations. For participants <18 years, parents, husbands, or guardian gave informed permission and assent was obtained from the participants. Privacy and confidentiality of medical information were protected during and after the study.

Patient and Public Involvement

We followed national guidelines to get overall patient and public involvement guidance, and tailored visits for data collection according to best practice and local engagement. Written assent of participants was gotten in their homes.

Study Setting

This study was carried out across a sub-group of girls and women residing in remote fishing communities in the Matta Health Area in the West Region of Cameroon, around the Mape Dam, a known transmission focus for *Schistosoma haematobium*[11, 16]. Apart from reporting symptoms for UGS such as blood in urine, for FGS specifically included vaginal itch and smelly discharge, lower abdominal pain, painful coitus, missed periods and miscarriages[17]. As previously detailed, all study participants were involved actively in fishing or other household activity that put them in constant contact with the lake water,[17]. Of note, the Matta Health Area hosts several remote fishing island communities that surround the man-made barrage (Mape Dam), and for at least 18 years has witnessed high transmission of *S. haematobium* with prevalence of UGS in children greater than 50%[18].

Study Design and Procedures

This observational cross-sectional survey was conducted between the periods of December 2020 to June 2021. The total population estimate of the study site was 5,000 people[19], where women represented 51.0% of the population, with the age group 15-64 years representing 54.6% of the total population. Using a simple random sampling technique, on the base of attaining a precision rate of 95% with an error margin of 5%, our initial sample size was estimated statistically using the population proportion formula n = N*X / (X + N – 1), where, X = Zα/2 ¬*p*(1-p) / MOE2, and Zα/2 is the critical value of the normal distribution at α/2 (for the confidence level of 95%, α is 0.05 and the

critical value is 1.96), MOE is the margin of error (5%), p is the sample proportion (55%), and N is the population size (1400), giving a required sample size of 387. This was later attained with a 85% success rate[17] due to logistic and cultural limits. Of the 304 participants originally sampled and tested for UGS, a sub-group of 67 women and girls from an unbiased selection with explicit inclusion and exclusion criteria underwent clinical gynecological examination (for FGS) by colposcopy with photo documentation. For this sub-group an exclusion criteria of: age (>13 years), virginity status (not virgin), menstruation (not in current menses), and pregnancy (not pregnant), was applied alongside obtaining consent for gynecological exam (Fig 1), by a trained gynecologist with previous experience in diagnosing FGS.

Figure 1: Study participant selection criteria and numbers with diagnostic methods flow

A structured questionnaire (see Supplementary File 1) with FGS related symptoms, sexual and reproductive health, and socio-demographic questions was administered privately in a one-to-one format. On average interviews were completed during 35 minutes and were conducted after the urine was collected from each study participant. Each participant responded to the structured questionnaire and was prompted to discuss further on related symptoms if they wished to share, but these were not formally registered by the questionnaire.

Participants were selected for gynecological examination based on having a UGS urine test performed and having a completed response to questionnaire concerning FGS symptoms and water contact activity. Sexual and reproductive health questions included : sexual activeness, age at mariage, number of children, age of last child, any miscarriage, menstrual irregularities or abnormalities. Demographic questions asked included: age, level of formal or informal schooling achieved, water contact activities, and income generating activities. Most females encountered were married by age14, which helped guide the minimum age band set for the study. To better explore age-related profiles, three age sub-groups were formed: adolescence (14-19), young adults (20-35) and older adults (36+).

Parasitological and Gynecological Examinations

At least 10 ml of urine was collected and analyzed by visual inspection for macrohaematuria and then tested for microhaematuria and proteinuria with reagent strips (Siemens Multistix 10 SG) at the local health center laboratory on the same day of collection. Urine syringe filtration technique was performed with visualization of schistosome eggs by x100 using a light compound and stained with Lugol's iodine. A sample was deemed positive for *S. haematobium* if at least one terminal-spined ovum was seen, and the number of ova reported as per ≥50 (high intensity) or < 50 (low intensity). Next, consenting eligible girls and women were examined by clinical colposcopy with photo-documentation, using a hand held colposcope (EVA COLPO, Mobile ODT). The obtained images were cross-checked against the WHO FGS pocket atlas[20] to record key sequelae. These were then saved in a coded database, accessible to predetermined independent experts. An FGS positive case was declared upon the presence of either sandy patches, abnormal blood vessels and sandy patches on homogenous yellow areas in line with the WHO FGS pocket atlas coding[20].

Statistical Analysis

All numerical data on girls and women examined for FGS (n = 67) were extracted from the main database in Excel and imported into the R (version 4.0.2) software for statistical analyses. In univariate analysis, frequencies and proportions were reported for socio-demographic characteristics. In bivariate analysis, Pearson's chi-squared tests were used to test the dependence of reproductive health related independent variables against FGS or UGS (dependent variables). To further explain such dependence, univariate logistic regression analyses was used, with the results presented in the form of unadjusted odds ratios. To identify amongst the reproductive health related independent variables associated to UGS and FGS, multivariate logistic regressions analyses were used, with the results presented in the form of adjusted odds ratios (AOR), alongside 95% confidence intervals (CI) and p-values based on the Wald's Test. To fit the models, only factors significantly related to the outcomes at a 25% level of significance in the univariate models were included. Multicollinearity between independent variables was tested using the variance inflation factor. The forward-backward stepwise selection method was used to obtain the " best" fitting models. Analysis of deviance tables

accompanied by likelihood ratio tests were used to assess the global significance of the different variables in the final statistical models. In all, the level of significance was set at $p<0.05$.

Results

i. Demographic Characteristics of Participants

Analysis was restricted to the 67 post-menarche sexually active girls and women above the age of 13 who gave informed consent for and participated in full for all aspects of the study. Participants were classified into 3 age-groups: adolescents (14 -19 years); young adults (20-35 years); and older adults (36+ years). Table 1 presents a summary of the socio-demographic characteristics (age-group, residence, marital status and water contact history) of the study participants. The median age was 21 years; interquartile range [IQR] 18–25, whereadolescents represented 28.4% of the study participants, young adults 43.3%, and older adults 28.4%.

Table 1: Participant Characteristics

Socio-demographical characteristics		
Age group (N= 67)	**N**	**Proportion**
14-19	19	28.4%
20-35	29	43.3%
36+	19	28.4%
Economic activity (N= 67)		
Fishing	31	46.4%
Farming	03	4.5%
Fishing/Farming	33	49.3%
Proximity to lake (N= 67)		
< 200m	07	89.6%
≥200m	60	10.4%
Marital status (N= 67)		
Married	66	98.5%
Widowed	1	1.5%

None of the 67 participants had completed primary level of education (formal education), all had completed a cultural training (informal education) considered as a requisite for socialization and marriage. Over 98% of participants were currently married, about 35% by the age of 14, and the

remainder after the age of 15. The main occupations were fishing and farming (49.3%), fishing (46.3%), and farming only (4.5%).

Of the total number of participants (n=67), 40 were confirmed to have ova-patent UGS, and 34 for FGS upon the presence of homogenous yellow sandy patches, grainy sandy patches and abnormal blood vessels. One participant was noted to have rubbery papules, a condition previously thought to be restricted to Madagascar, and is the first time this condition has been reported in Cameroon (Fig 2).

Figure 2 : Imagery of FGS pathology of the cervix with reported lesions (magnification of x4)

A) 1-rubbery papule, 2-abnormal blood vessel, 3- homogeneous sandy patch (30 year old woman, +UGS, +lower abdominal pain, +Menstrual irregularity) ; **B**) 1,2- grainy sandy patches (45 year old woman, -UGS, +lower abdominal pain ; +Menstrual irregularity)

ii. UGS, FGS and associations with reproductive health characteristics

Age, number of children, age of last child, menstrual abnormality, miscarriages, and lower abdominal pain were identified as possible reproductive health factors associated with *S. haematobium* infection, and were used within this study. Table 2 presents UGS, FGS and their relationship with these reproductive health characteristics, based on chi-square tests of independence on one hand, and univariate logistic regression on the other. Generally, both FGS and UGS were not significantly (*P*-value >0.05) related to number of children, age of last child and miscarriages. However, a significant relationship between FGS and age group (P=0.009 X^2 *test*) and menstrual abnormality (P=0.005X^2 *test*) was observed, while both FGS (P=0.001 X^2 *test*) and UGS (P=0.023 X^2 *test*)were observed to be significantly associated with lower abdominal pain. In effect, the probability of infection with FGS was seen to increase with age, with unadjusted odds ratios (UOR) of 6.4 (95% C: I 1.6-30.4) for older adults, 6.1 (95% CI: 1.7-26.1) for young adults, relative to adolescents as reference category. On the other hand, a non-significant decrease in chances of infection with urogenital schistosomiasis was

observed with increasing age. Furthermore, the chances of FGS infection amongst girls with menstrual abnormality (collected as irregular, painful or ceased menstruation), was UOR 7.1(95% CI: 2.5-22.1) times that for girls without the abnormality. Chances of FGS infection amongst women with lower abdominal pain, was 17.1 (95% CI: 4.2-117.1) times that of women without lower abdominal pain. A similar trend was observed with UGS, but on a lower scale [UOR 4.3 (95% CI: 1.4-14.4)].

Additionally, a non-statistically significant increase in prevalence of menstrual abnormalities was observed with increasing age (X^2=1.51, df=2, p-value=0.469). In effect, the prevalence of menstrual abnormalities amongst adolescents was 44.4%, young adults 48.3%, and older adults 63.2%.

Table 2: Associations of certain sexual and reproductive health characteristics between UGS and FGS: Univariate logistic regression model on the effects of UGS and FGS on sexual and reproductive health factors and on the probability of contracting FGS after UGS

SRH Indicator	Category	FGS					N	UGS				
		Chi2 Test of Independence			Univariate logistic regression			Chi2 Test of Independence			Univariate logistic regression	
		FGS + n(%)	FGS - n(%)	P value	Unadjusted OR (95% C.I.)	P value		UGS + n(%)	UGS - n(%)	P value	Unadjusted OR (95% C.I.)	P value
Age group	13-19	4 (11.8)	15 (45.5)	**0.009**	1.0		*19*	13 (32.5)	6 (22.2)	**0.439**	1.0	
	20-35	18 (52.9)	11 (33.3)		6.1 (1.7, 26.1)	0.008	*29*	18(45)	11(40.7)		0.8 (0.2, 2.5)	0.653
	36+	12 (35.3)	7 (21.2)		6.4 (1.6, 30.4)	0.012	*19*	9(22.5)	10(37)		0.4 (0.1, 1.5)	0.192
Number of Children	None	4 (11.8)	9 (30)	**0.107**	1.0		13	9(24.3)	4(14.8)	**0.185**	1.0	
	1-3	10 (29.4)	12 (40)		1.8 0.5, 8.7)	0.394	22	12(32.4)	10(37)		0.5 (0.1, 2.)	0.394
	4-6	11 (32.4)	4 (13.3)		6.2 (1.3, 36.1)	0.030	15	11(29.7)	4(14.8)		1.2 (0.2, 6.6)	0.811
	7+	9 (26.5)	5 (16.7)		4.1 (0.9, 22.3)	0.088	14	5(13.5)	9(33.3)		0.3 (0.0, 1.2)	0.088
Age of last child	1-3	13(46.4)	15(71.4)	**0.115**	1.0		28	14(53.8)	14(60.9)	**0.188**	1.0	
	4-6	4(14.3)	0(0)		Inf	0.993	4	4(15.4)	0(0)		Inf	0.993
	7+	11(39.3)	6(28.6)		2.1 (0.6, 7.7)	0.237	17	8(30.8)	9(39.1)		0.9 (0.3, 2.9)	0.848
Menstrual abnormality	No	9(26.5)	23(71.9)	**0.005**	1.0		32	17(43.6)	15(55.6)	**0.453**	1.0	
	Yes	25(73.5)	9(28.1)		7.1 (2.5, 22.1)	<0.001	34	22(56.4)	12(44.4)		1.6 (0.6, 4.4)	0.340
Miscarriages	0	8(23.5)	15(50)	**0.104**	1.0		23	11(29.7)	12(44.4)	**0.211**	1.0	
	1	14(41.2)	8(26.7)		3.3(1.0, 11.7)	0.057	22	16(43.2)	6(22.2)		2.9(0.9, 10.7)	0.093
	2+	12(35.3)	7(23.3)		3.2(0.9, 11.9)	0.071	19	10(27)	9(33.3)		1.2 (0.4, 4.2)	0.757
Lower abdominal pain	No	2(5.9)	16(51.6)	**0.001**	1.0		18	6(15.8)	12(44.4)	**0.023**	1.0	
	Yes	32(94.1)	15(48.6)		17.1 (4.2, 117.1)	0.001	47	32(84.2)	15(55.6)		4.3(1.4, 14.4)	0.014
Parasitaemia (egg density)	0	10(29.4)	17(51.5)	**0.172**	1.0		27					
	1-49	15(44.1)	9(27.3)		2.8 (0.9, 9.2)	0.073	24					
	50+	9(26.5)	7(21.2)		2.2 (0.6, 7.9)	0.224	16					

*Inf signifies very large odds ratio

iii. Multivariate Logistic Regression Model for Reporting Reproductive Health Risk Factors

Multicollinearity was observed between age group, number of children and age of last child, and so we resorted to excluding number of children and age of last child in the multivariate model. Multivariate logistic regression analyses results for identifying associates amongst reproductive health characteristics to both FGS and UGS infections are given in Table 3. After selection of the best fitting models, the results show that the only significant risk factor for UGS is lower abdominal pain, whereas age-group and lower abdominal pain were identified as the two main significant risk factors for FGS. In the same line as with the Univariate regression results in Table 2, the probability of infection with female genital schistosomiasis was seen to increase with age, with adjusted odds ratios (AOR) of 7.7 (95% CI: 1.4-55.7) for older adults, 5.9 (95% CI: 1.3-34.3) for young adults, relative to adolescents as reference category.Chances of FGS infection amongst women with lower abdominal pain was AOR 9.5(95% CI:1.7-81.8) times that of women without the pain. Analysis of deviance tables for both best fitting models (FGS and UGS), with *p*-values based on likelihood ratio tests are reported in Table 4.

Table 3: Key risk factors amongst SRH between UGS and FGS. A multivariate logistic regression model on the effects of UGS and FGS on sexual and reproductive health factors and on the probability of contracting FGS after UGS.

SRH Indicator	Category	FGS			UGS	
		Multivariate Logistic Regression			Multivariate Logistic Regression	
		Adjusted OR (95% C.I.)	P value		Adjusted OR (95% C.I.)	P value
Age group	14-19	1.0			//	
	20-35	5.9 (1.3, 34.3)	0.032		//	//
	36+	7.7 (1.4, 55.7)	0.027		//	//
Menstrual abnormality	No	1.0			//	
	Yes	3.9 (1.0, 16.7)	0.056		//	//
Lower abdominal pain	No	1.0			1.0	
	Yes	9.5 (1.7, 81.8)	0.017		4.3 (1.4, 14.4)	0.014

// signifies that variable was not considered in the best fitting model

Table 4: Analysis of deviance tables showing the global significance of the different variables in the best fitting models.

Variable	Df	Deviance	Resid. df	Resid. Dev	*P*-value
1. FGS					
Age-group	2	7.916	62	82.050	0.019
Menstrual abnormality	1	14.024	61	68.031	<0.001
Lower abdominal pain	1	7.010	60	61.021	0.008
2. UGS					
Lower abdominal pain	1	5.846	61	80.201	0.016

Discussion

Our study, given our application of portable colposcopy, is the first formal attempt to document the pathology of FGS in a primary care setting in Cameroon. Elsewhere, the clinical pathology of FGS has been described resulting from the complex inflammatory responses to antigens released by adult worms and viable eggs, which persists until some time after adult worms are stopped egg-laying or are destroyed by praziquantel[21]. Thereafter, various signs and symptoms may present months or even years after treatment[22]. Though a non-significant association (P=0.172) was observed between egg intensity in urine and FGS from the onset of this study (Table 2), parasitaemia association has been shown to be misleading from several other studies and reports on FGS, particularly when only a single urine sample is examined which is usually the case for population-based surveillance[3]. The possibility of the presence of FGS in UGS populations has been often raised[6, 23],with projections of about 360 million girls and women possibly infected with UGS but today it is thought that at least 56 million adolescent girls and women are suffering from FGS[24, 25]. Our results maybe show an even higher rate of FGS infection amongst the UGS infected population with an approximate FGS/UGS ratio of 34/40.

From present results, and within the general literature[24, 25], one of such effects noted is an effect on menstrual health. More than half of women within the study who reported poor menstrual health (FGS = 73.5% ; UGS = 54.6%), either as irregular, painful or seized menstruation, were found to either shed eggs in urine (positive for UGS), or were positive for FGS, but without eggs in urine. A significant trend was seen with more women positive for FGS reporting abnormal menstruation, than for UGS.

This confirms recent analysis suggests strong linkages between menstrual health management and FGS[24], an under researched area. In our study post-menarche females already faced a substantial challenge with limited access to hygienic material and information on menstrual health management, typically relying on self made clothes and absorbent plant leaves during menstruation, due to lack of finances or general knowledge. Also an increase (though non-significant) in menstrual abnormality was recorded with increasing age-group, where older adults (36+) experienced more abnormalities than the younger women who in-turn observed higher abnormalities than adolescents. This can be credited to the fact that symptoms perhaps diminished after a while with UGS (maybe as a result of treatment in mass drug administration campaigns), but later resurface with more chronic sequelae of FGS, and with more dire symptoms and negative impact on mental health[24].

To affirm this, narratives from a previous study which used qualitative probing showed women infected with FGS and not shedding eggs in urine, gave a history of having lived in their earlier years in heavily infested *S.haematobium* foci, which explained their later manifestation of FGS symptoms, even after having moved away to a less infested area, with more than 90% limit in fresh water contact[17]. The significant difference in menstrual abnormalities amongst UGS positive women [n=22(56.4)] and UGS negative women [n=12 (44.4)], alerts to future chronicity of FGS after infection with UGS, especially if not managed with praziquantel treatment(s). This implies the need for early management with more readily available praziquantel treatment for UGS to avoid future risks of FGS[22, 26].

On its own, lower abdominal pain observed significant association (in adjusted and unadjusted regression models) in both UGS and FGS infections. The chances of having lower abdominal pain was significantly higher in females with either FGS (94.1%) or UGS (84.2%). This reported as key indicator for UGS and FGS, directing early diagnosis of UGS and future FGS in endemic communities, promoting the verticalization of control strategies for both diseases.

Another trend observed in this study is that intensity of infection or egg patent-prevalence (for UGS) reduces while chronic disease or morbidity for FGS increases as women age. Since women aged (36+), chances of infection with FGS after infection with UGS increased significantly (AOR 6.43,95%

C.I 1.62-30.35, P=0.0091), similarly reported in other studies in different geographical locations[3, 27-29] and recently in this area[17]. This diverts once small from the two most common hypothesis of age and infection for *S.haematobium* infection[30]; emphasizing on the level of present intensity of infection for UGS, and possible future occurrence of FGS[28, 29].This age-infection association in both UGS and FGS, is highlighted further in the Multivariate model here, where emphasise on infection history for UGS and FGS is seen more clearly. UGS at a younger age will in some cases manifest into FGS when the female is older, causing more intense gynecological symptoms and effects. This offers a possible guiding tool for better control policies, related to early diagnosis and treatment[31, 32]. This surpasses need alone for school-based MDAs, but considers and encourages individual therapy in different contexts for FGS (and MGS)[3]. Also, these results support the advocated need for availability of praziquantel in lowest level (health areas and community) Health Centers for individual therapy[29], as well as treatment from a younger age[25, 26, 32, 33] buoyed with the recent development of pediatric praziquantel[34].

Although only a few amongst the extensive list of reproductive health determinants were identified in this study to be statistically significant, where mostly reported symptoms were collected, clinical and biological examinations carried out, enabled confirmation of how future self-reported symptoms with UGS and FGS might be best used[17].

Conclusion

In our chosen study location, which is broadly typical for endemic areas of UGS in Cameroon, strong epidemiological associations between UGS and FGS were found against certain key sexual and reproductive determinants: age, lower abdominal pain and menstrual health. This formative knowledge could be utlised to tackle and ultimately prevent FGS, with a more targeted integrated control for UGS in Cameroon and elsewhere in endemics areas for UGS in sub-Saharan Africa.

Supporting Files

Supplementary File 1.docx : Structured questionnaire

Declarations

- **Authors' contributions**

MCM and JRS conceptualized the study and planned the methodology; VAG, MCM, NTM, carried out field investigation; MCM, FNB, JRS, ASO analysed and interpreted the data for this manuscript; MCM acquired funding for study and wrote the original draft of the manuscript; JRS supervised the study and was a major contributor in the conceptualization and writing of the manuscript; FNB, VG, NTM, ASO, reviewed and edited the manuscript. All authors approved the final version of the paper before submission**.**

- **Competing interests**

The authors declare that they have no competing interests.

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- **Data Sharing Statement**

All data generated or analyzed during this study are included in this published article [and its supplementary files].

- **Acknowledgements**

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- **Consent for publication**

Written informed consent for publication of clinical details and/or clinical images was obtained from the patients and parents/guardians where needed.

References

1. Poggensee G, Kiwelu I, Saria M, et al. Schistosomiasis of the lower reproductive tract without egg excretion in urine. *Am J Trop Med Hyg*. 1998;59(5):782-3.
2. Ekpo U, Odeyemi O, Sam-Wobo S, et al. Female genital schistosomiasis (FGS) in Ogun State, Nigeria: a pilot survey on genital symptoms and clinical findings. *Parasitol Open*. 2017;3:e10.
3. Kjetland E, Leutscher P, Ndhlovu P. A review of female genital schistosomiasis. *Trends Parasitol*. 2012;28(2):58-65.
4. Bustinduy AL, Randriansolo B, Sturt AS, et al. An update on female and male genital schistosomiasis and a call to integrate efforts to escalate diagnosis, treatment and awareness in endemic and non-endemic settings: The time is now. In: Rollinson D, Stothard R, editors. *Adv Parasitol*. 115: Academic Press; 2022.p.1-44.
5. Stothard J. Female genital schistosomiasis - icebergs of morbidity ahead? *Trends Parasitol*. 2012;28(5):174-5.
6. Campbell S, Stothard J, O'Halloran F, et al. Urogenital schistosomiasis and soil-transmitted helminthiasis (STH) in Cameroon: An epidemiological update at Barombi Mbo and Barombi Kotto crater lakes assessing prospects for intensified control interventions. *Infect Dis Poverty*. 2017;6(1):49-49.
7. King C. Parasites and poverty: the case of schistosomiasis. *Acta Trop*. 2010;113(2):95-104.
8. Kjetland EF, Mduluza T, Ndhlovu PD, et al. Genital schistosomiasis in women: a clinical 12-month in vivo study following treatment with praziquantel. *Trans R Soc Trop Med Hyg*. 2006;100(8):740-52.
9. World Health Organisation. WHO guideline on control and elimination of human schistosomiasis. https://www.who.int/publications/i/item/9789240041608: WHO; 2022. p.142. [Accessed 10/03/2022].
10. SCI Foundation. FAST PACKAGE PROJECT 2021[Available from: https://schistosomiasiscontrolinitiative.org/projects/fast-research-project [Accessed 31/01/2022].

11. National Program for the control of Schistosomiasis and intestinal helminthiasis MoPHC. Towards elimination of Schistosomiasis and Soil-transmitted Helminthiasis and in Cameroon: A road map for paradigm shift 2021-2030. MINSANTE, Yaoundé:[Available from https://www.eliminateschisto.org/resources/2021-2030-road-map-schistosomiasis-sth-cameroon]Accessed 12/01/ 2022.

12. World Health Organization. Global update on implementation of preventive chemotherapy against neglected tropical diseases in 2018. *Wkly Epidemiol Rec*. 2019;94(38):425-38.

13. Crompton DWT, World Health Organization. Preventive chemotherapy in human helminthiasis : coordinated use of antihelminthic drugs in control interventions : a manual for health professionals and programme managers. Geneva: World Health Organization; 2006.[https://apps.who.int/iris/handle/10665/43545]Accessed 12/02/2022

14. National Program for the control of Schistosomiaisis and intestinal helminthiases. Progress Report Cameroon 2013-2019. Yaoundé: MINSANTE; 2019.[https://www.eliminateschisto.org/resources/cameroon-2003-2019-progress-report-towards-elimination-of-schistosomiasis-and-sth-in]Accessed 13/01/2022.

15. Makia C, Ozano K, Tagne M, et al. Achieving equity in UHC interventions: who is left behind by neglected tropical disease programmes in Cameroon? *Glob Health Action*. 2021;14(1):1886457-.

16. Njunda A, Ndzi E, Assob J, et al. Prevalence and factors associated with urogenital schistosomiasis among primary school children in barrage, Magba sub-division of Cameroon. *BMC Public Health*. 2017;17(1):618.

17. Masong MC, Wepnje GB, Marlene NT, et al. Female Genital Schistosomiasis (FGS) in Cameroon: A formative epidemiological and socioeconomic investigation in eleven rural fishing communities. *PLOS Glob Public Health*. 2021;1(10):e0000007.

18. MINSANTE. Schistosomiasis distribution in Malanteoun Health District NTDmaps.org: MINSANTE; 2018 [Available from: https://ntdmaps.org/.]Accessed 2022.

19. National Institute of Statistics Cameroon. Socio-economic statistics of Cameroon, 2015 Cameroon 2004-2014 [Available from: https://cameroon.opendataforafrica.org/SESC2015/socio-economic-statistics-of-cameroon-2015.Accessed 3/02/2022.

20. WHO. Female Genital Schistosomiasis: A Pocket Atlas for Clinical Health-Care Professionals Geneva: WHO Press; 2015 [Available from: https://www.who.int/publications/i/item/9789241509299. Accessed 13/01/2022

21. Treatment of Female Genital Schistosomiasis (FGS) With Praziquantel: A Proof-of-Concept Study (NCT04115072) [Available from: https://clinicaltrials.gov/ct2/show/NCT04115072]. NIH: ClinicalTrials.gov archive. 2020[cited 31/01/2022].

22. Nour NM. Schistosomiasis: health effects on women. *Rev Obstet Gynecol*. 2010;3(1):28-32.

23. Christinet V, Lazdins-Helds J, Stothard J, et al. Female genital schistosomiasis (FGS): from case reports to a call for concerted action against this neglected gynecologicaldisease. *Int J Parasitol*. 2016;46(7):395-404.

24. Stothard JR, Odiere MR, Phillips-Howard PA. Connecting Female Genital Schistosomiasis and Menstrual Hygiene Initiatives. *Trends Parasitol*. 2020;38(5).

25. UNAIDS. 'No more neglect:Female genital schistosomiasis and HIV. www.unaids.org/en/resources/documents/2019/: UNAIDS; 2019.Accessed 13/01/2022.

26. Bustinduy AL, Friedman JF, Kjetland EF, et al. Expanding Praziquantel (PZQ) Access beyond Mass Drug Administration Programs: Paving a Way Forward for a Pediatric PZQ Formulation for Schistosomiasis. *PLoS Negl Trop Dis*. 2016;10(9):e0004946.

27. Chetty A, Omondi MA, Butters C, et al. Impact of Helminth Infections on Female Reproductive Health and Associated Diseases. *Front Immunol*. 2020;11:577516.

28. Hegertun I, Gundersen S, Kleppa E, et al. *S. haematobium* as a common cause of genital morbidity in girls: a cross-sectional study of children in South Africa. *PLoS Negl Trop Dis*. 2013;7(3):e2104.

29. Stothard JR, Stanton, M, Bustinduy, A, et al. Diagnostics for schistosomiasis in Africa and Arabia: A review of present options in control and future needs for elimination. *Parasitology*. 2014(141):1947-61.

30. Feldmeier H, Poggensee G, Krantz I. Puberty and Age-intensity Profiles in Schistosome Infections: Another Hypothesis. *Parasitol Today*. 1998;14(10):435;

31. Richardson ST, Franklin AL, Rome ES, et al. Global Health: Urogenital Schistosomiasis in the Adolescent Girl. *J Pediatr Adolesc Gynecol*. 2016;29(4):326-32.

32. Deworming adolescent girls and women of reproductive age. Policy Brief [press release]. Geneva: WHO 2022. [Avaialable from: https://www.who.int/publications/i/item/9789240037670]Accessed 11/03/2022.

33. Faust CL, Osakunor DNM, Downs JA, et al. Schistosomiasis Control: Leave No Age Group Behind. *Trends Parasitol*. 2020;36(7):582-91.

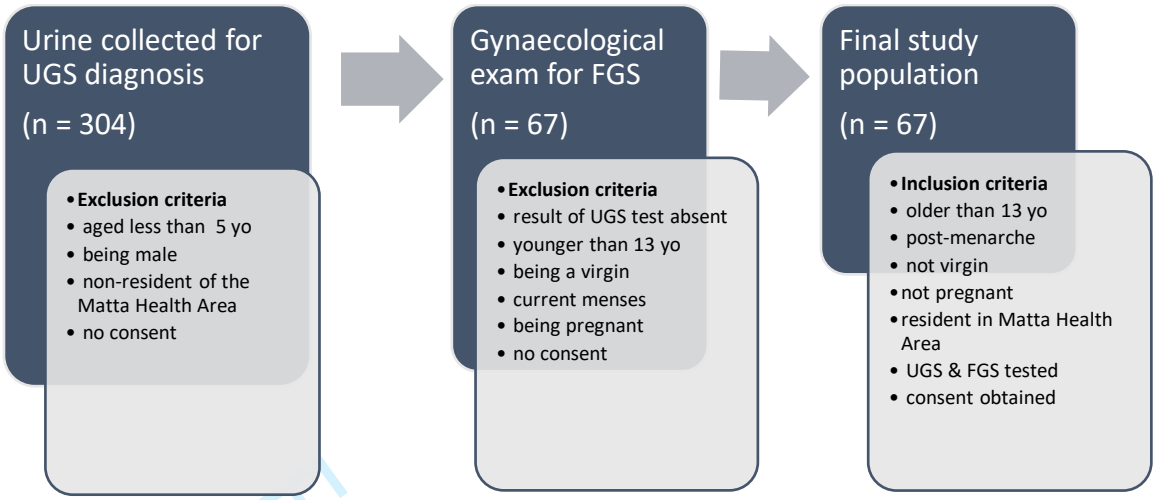
34. Pediatric Praziquantel Consortium. Contract manufacturing agreement signed for production of new pediatric treatment for schistosomiasis 2021[Available from: http//:https://www.pediatricpraziquantelconsortium.org/ Accessed 10/01/2022.

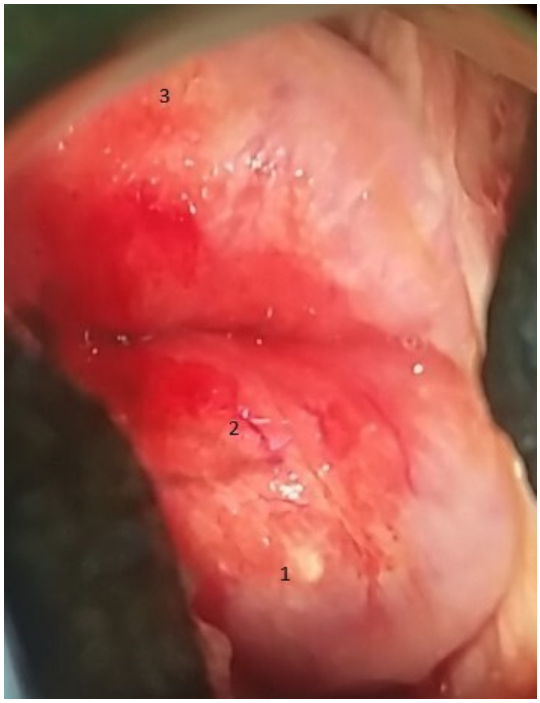
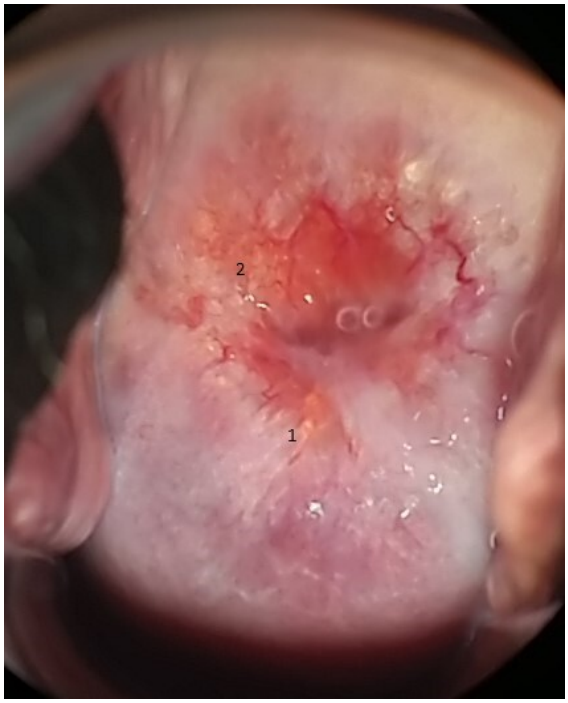
- **Figure Legends**

Figure1: Study participant selection criteria and numbers with diagnostic methods flow

Figure 2 : Imagery of FGS pathology of the cervix with reported lesions (magnification of x4)

A) 1-rubbery papule, 2-abnormal blood vessel, 3- homogeneous sandy patch (30 year old woman, +UGS, +lower abdominal pain, +Menstrual irregularity) ; **B**) 1,2- grainy sandy patches (45 year old woman, -UGS, +lower abdominal pain ; +Menstrual irregularity)



A	B
	

Supplemantary File 1

Close-ended structured questionnaire

A. Close ended structured questionnaire– Administered directly in English with oral translations into Fulbe, Kotoko, Mosgum, and Arab

Name of Community: _____

Age (years): _____

Education: Informal education () Formal education () (specify)_____

Marital Status: Single ( ) Married ( ) Separated ( ) Widowed ( )

No of years having lived in community _____

Previous community _____

Economic activity----------

Residence ---------- (collect coordinates)

Questions on symptoms of urinary tract schistosomiasis; FGS; OR STI

1. Do you see your menses? Yes ( ) No ( )
2. Did you observe/experience your menses within the last two weeks? Yes ( ) No ( ) Does your menses come every month? Regular?
3. Is your menses painful? _____(pain during menstruation – always very painful, sometimes painful, normal) Irregular? _____(every month?, not every month, stopped)
4. Do you have pain in your lower abdomen? When? For how long?
5. Do you have pain when urinating? Yes ( ) No ( )
6. Do you have difficulty in urinating (urine not coming out fluently)? Yes ( ) No ( )
7. Do you have sudden uncontrollable and unexpected urge to urinate and mostly cannot hold it? Even when you cough it comes out? Yes ( ) No ( )
8. Do you see blood in your urine? Yes () No ()
9. (If yes) When did you lastly see blood in your urine? _____Always, sometimes, Once in a while
10. Do you sometimes haveitching in your private part?Yes ( ) No ( )
11. How often do you experience this? Once a while ( ) frequently ( )/ When was the last time?
12. Do you have a feeling of burning within your private part? Yes ( ) No ( )

13. How often do you experience this? Once a while ( ) Frequently ( )

14. Do you sense a swelling/lumps within your private part? Yes ( ) No ( ) No response ( )

15. Do you have any discharge that comes from your vagina? Yes () No () Does it have an ordure? _____ Do you see the colour? Yes ( ) No ( ) What Color is it?White; grey; green/yellow; brown

16. Do you think this is normal? Yes () No() Do not know(). When did you start observing the discharge? Date _____

17. After sexual intercourse do you have a discharge? Yes () No () Is it smelly? Yes () No () Do not know ()

18. After or during sexual intercourse do you have pain?Yes ( ) No ( ) I do not know ( ) ; Do you have a bloody discharge?Yes ( ) No ( ) I do not know ( )

19. Have you had any miscarriages /pregnancies that passed? Yes ( ) No ( )

20. How many? ()

21. Do you have children? Yes() No()

22. What age is your last child? ()

23. Have you visited the clinic to complain about these issues? Yes ( ) No ( )

24. What you used/taken/done to treat any of these problems? _____ (Underline) Hospital or drug store/ local midwife/ traditional medicine/ prayers/ none of the above (what other? Specify)/nothing

Water contact History

1. Where do you fetch your household water? Lake; other source (name) _____
2. Do you fish in the lake? Yes (), No ()
3. Do you bathe in the lake? Yes (), No ()
4. What do you use the lake for? ()_____

BMJ Open

Urogenital Schistosomiasis (UGS) and Female Genital Schistosomiasis (FGS) in Cameroon: An observational assessment of key reproductive health determinants of girls and women in the Matta Health Area

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Title: Urogenital Schistosomiasis (UGS) and Female Genital Schistosomiasis (FGS) in Cameroon: An observational assessment of key reproductive health determinants of girls and women in the Matta Health Area

Authors: Makia Christine Masong[1*], Fesuh Nono Betrand[2], Amabo Elvis Ngwa[3], Victoria A. Gamba[4], Akinola Stephen Oluwole[5], J. Russell Stothard[6]

[1]Department of Social Sciences and Management, Catholic University of Central Africa, Yaoundé, Cameroon

[2]Department of Mathematics and Physical Sciences, National Advanced School of Engineering, University of Yaoundé 1, Cameroon

[3]Malanteoun Health District, Malanteoun, Cameroon

[4]Department of Obstetrics and Gynecology, University of Nairobi, Nairobi, Kenya

[5]Department of Pure and Applied Zoology, Federal University of Agriculture, Abeokuta, Nigeria

[6]Department of Tropical Disease Biology, Liverpool School of Tropical Medicine, Liverpool, L3 5QA, UK

*Corresponding author

Makia Christine Masong

Department of Social Sciences and Management, Catholic University of Central Africa, Yaoundé, Cameroon

Projet MTN/OCEAC

masongbye@yahoo.com

Abstract

Objectives and Setting: Across sub-Saharan Africa, Urogenital Schistosomiasis (UGS), in particular Female Genital Schistosomiasis (FGS) is a significant waterborne parasitic disease, with its direct burden upon the sexual and reproductive health (SRH) of sufferers infrequently measured. UGS has an established control plan, which in most endemic regions as in Cameroon, still excludes FGS considerations. Highlighting existent associations between UGS and FGS could increase the management of FGS within UGS interventions. This study seeks to identify current associations amongst FGS and UGS with some reproductive health indicators, to provide formative information for better integrated control.

Participants: 304 females aged 5- 69 years, were all examined for UGS by urine filtration and microscopy. Amongst these, 192 women and girls were eligible for FGS assessment based on age (>13). After questioning for FGS symptoms, a sub-group of 67 women and girls from this population consented for clinical assessment for FGS through application of portable colposcopy, with observed sequelae classified according to the WHO FGS pocket atlas.

Outcome: Overall UGS and FGS prevalence was measured, with FGS/UGS related reproductive health symptoms recorded. Epidemiological associations with FGS and UGS were investigated by univariate and multivariate logistic regression analyses.

Results: Overall UGS prevalence was 63.8% (194/304), where FGS prevalence (sub group) was 50.7% (34/67). FGS increased significantly with increasing age, whilst a non-significant decrease with descending age was observed for UGS. Lower abdominal pain (LAP) vaginal itches (VI), and coital pain (CP), were identified as the main significant shared symptoms of both FGS and UGS, while LAP with MI appeared a strong epidemiological flag for FGS.

Conclusion: LAP, MI, CP and VI provide under-explored dimensions in SRH that could be exploited in future for targeting of praziquantel provision to FGS sufferers within primary care, complementary with existing distribution for UGS sufferers in *S. haematobuim* endemic areas.

Keywords: *Schistosoma haematobium*, SRH, clinical colposcopy, questionnaires, menstrual health, abdominal pain

Strengths and Limitations of this study

- Using clinical colposcopy, a not very common tool within primary health care settings in sub-Saharan Africa, combined with an analysis of sexual and reproductive health determinants, we identify existing relationships with symptoms of FGS and UGS affecting the sexual and reproductive health of women in sub-Saharan Africa, which could inform the development of a simple questionnaire approach to better capture FGS sufferers within endemic areas for UGS.

- Here, formative evidence is provided with initial recommendations, towards developing better national surveillance and control of FGS, thereby better empowering women's health within low resource settings, especially where schistosomiasis is endemic.

- This study did not consider clinical diagnosis of girls younger than 14, especially as non-invasive clinical diagnostic tools are lacking for examination amongst this age group within low resource schistosomiasis endemic communities.

- Assessment for STIs amongst participants are not presented here, where such results could complement or clarify FGS diagnosis, considering most sexual and reproductive health related symptoms for urogenital schistosomiasis present as sexually transmitted infections, and can be misdiagnosed.

Introduction

In endemic areas, a definitive diagnosis of Urogenital schistosomiasis (UGS) is established by demonstration of viable *Schistosoma (S) haematobium* eggs (≥1) in urine and/haematuria[1, 2], whilst

female genital schistosomiasis (FGS) can be diagnosed visually for *S. haematobium* induced cervical lesions and small fibrotic nodules known as "sandy patches"[2, 3], either with the presence or absence of *S. haematobuim* eggs in urine[1, 4, 5]. Whilst both FGS and UGS are caused by infection with *Schistosoma haematobium*[1, 6-8] a waterborne blood fluke, each appear to have some unclear epidemiological associations, largely due to insufficient disease surveillance[4, 5, 9, 10]. In sub-Saharan Africa where UGS is endemic and can be highly prevalent (>50%)[11, 12], insufficient or infrequent efforts have been undertaken to document FGS specifically[10, 13-15], partly as the clinical skills to do so are lacking and uninformed within primary care[9]. While active UGS does not readily predict FGS[4], since FGS can occur without the direct presence of schistosome eggs in urine (a cardinal diagnostic for UGS)[15, 16], rather FGS often presents with a more chronic time frame where schistosome eggs are trapped within the cervico-vaginal surfaces[4, 17, 18]. For some, these trapped eggs can accumulate from very early on in life[7], with enduring and typically hidden sequelae[17, 19]. Based on several biological determinants such as age[7], the mucosal damage and fibrotic scarring of the vaginal and cervical surfaces from FGS proceeds with increasing duration of UGS infection(s)[4]; moreover, FGS-specific sequelae maybe slow to resolve upon standard antiparasitic treatment of UGS[20, 21], i.e., single annual administration of praziquantel at 40mg/g as used in public health campaigns[4, 17].

In many parts of Africa where surveillance of UGS is limited[22] and that for FGS largely absent[12, 23], there is a clear need to better understand the epidemiological associations between UGS and FGS[11]. Particularly so, to support earlier diagnosis of cases of FGS, and individualize praziquantel treatment needs (for individual and context specific case management)[12, 24] to better avert their disease progression[12]; as current interventions against UGS do not specifically target adolescent girls or women[20, 25]. This gap in treatment coverage[24] also has considerable bearing on progress towards elimination of schistosomiasis transmission within disease endemic communities[25].

In recent years, FGS focused research and public health education[26] has gained traction in certain countries such as Ghana, Tanzania, Madagascar and Mozambique[6, 8], although other countries such

as Cameroon, currently lag behind[27, 28] Schistosomiasis exists in several regions of Cameroon[29], affecting over 10 million people in rural and urban areas[30]. The country has a national coordinated control plan for fairly early interventions during child-hood years (from 5 – 14 years old)[31], which take advantage of school based intervention platforms[32, 33], and in certain settings, with community based interventions, where their at-risk status (people or communities dependent on Schistosomiasis endemic water bodies, for main water source) is high[18, 27, 31, 34, 35]. Even with improved (>70%) helminth control amongst children in the last decade [30], some of the adolescent at-risk populations do not always benefit from praziquantel treatment due to existing policy gaps and program intervention challenges [[12, 36, 37].

To address this treatment deficit, capture missed opportunities, and ensure the consideration and apprehension of ensuing FGS manifestations within such already identified sub-groups (young girls and women); with better knowledge on the precise associations between UGS and FGS, future control policies and intervention campaigns can be revised to better target at-risk populations.

Here, we sought to clarify existing associations between FGS and UGS, highlighting cardinal symptomologies for scalable detection and targeted control of FGS within UGS endemic areas. This supports the need for a future integrated approach for control of Schistosomiasis and limits the "gap" concerning FGS surveillance within current primary care.

Materials and Methods

Ethics approval and consent to participate

Ethical clearance for this study was provided by the Cameroon National Ethics committee on Human Health Research (Ref N ° 2020/07/1266/CE/CNERSH/SP), with administrative authorizations from

both the Regional Delegation of Public Health for the West region of Cameroon (Ref N° 679/L/MINSANTE/SG/DRSPO/CBF), and the district Health Office of the Malanteoun Health District (Ref N° 078/L/MINSANTE/DRSPO/DSMLT). Informed written and oral consent was obtained from all participants for parasitological and gynecological examinations. For participants <18 years, parents, husbands, or guardian gave informed permission and assent was obtained from the participants. Privacy and confidentiality of medical information were protected during and after the study.

Patient and Public Involvement

We followed inclusive and participative methods to get overall participant and public involvement, where tailored visits for data collection were carried out according to best practices with local engagement of key community members and local health workers.

Study Setting

This study was carried out across a group of girls and women residing in remote communities in the Matta Health Area in the West Region of Cameroon, around the Mape Dam, a known transmission focus for *Schistosoma haematobium*[30, 35]. Most study participants were involved actively in fishing or other household activity that put them in constant contact with the lake water[28]. More than 90% of the population lived less than 200m to an endemic water source (the Mape Dam) and more than 75% depended fully on the Mape Dam for house-hold water and for an income generating activity (fishing) [28, 35]. Of note, the Matta Health Area hosts several remote fishing island communities that surround the man-made barrage (Mape Dam), and for at least 18 years has witnessed high transmission of *S. haematobium* with prevalence of UGS in children greater than 50%[38].

Study Design and Procedures

This cross-sectional study was conducted between the periods of December 2020 to June 2021. The total population estimate of the study site was 5,000 people[39], where women represented 51.0% of the population, with the age group 15-64 years representing 54.6% of the total population. With no existing records of schistosomiasis prevalence amongst adults within the Matta Health area, a hypothesis of UGS endemicity amongst adults was based on recorded school-age Schistosomiasis prevalence (> 41% in the

last decade) and within the Matta health Area [35, 38, 40]. Based on lake proximity and economic activity, 11 main communities were visited within the Matta Health Area: nine secluded water-locked fishing communities (Islands/fishing camps) with habitations mostly less than 200m from the lake; and two mainland communities (land-locked) with habitation more than 400m from the lake[28]. Following a simple random sampling technique, on the base of attaining a precision rate of 95% with an error margin of 5%, our initial sample size was estimated statistically using the population proportion formula[41]n = N*X / (X + N – 1), where, X = Zα/2 ¬*p*(1-p) / MOE2, and Zα/2 is the critical value of the normal distribution at α/2 (for confidence level of 95%, α is 0.05 and critical value is 1.96), MOE is the margin of error (5%), p is the sample proportion (55%), and N is the population size (1400)[28]. TheFinite Population Correction has been applied to the sample size formula.

Thus, n = 1400*3.8 / (3.8 + 1400–1), with n = 387. With an originally determined sample size of 387, due to logistic and cultural constraints, 304 (78.55%) of target recruitment was reached [28]. Due to the secluded nature of study communities (far from health care setting), and the preference of a participative nature for recruiting (involvement of formal/informal health workers and some community members), recruitment was contextualized within each community as per the propositions of key community members (including participants themselves). Of the 304 participants sampled and tested for UGS, 193 girls and women were eligible for FGS assessment (Figure 1). Eligibility criteria for clinical FGS diagnosis consisted: >13, non-virgin, not menstruating, not pregnant, and consent/assent from parent or spouse for girls younger than 18. Based on eligibility criteria, participant availability, and logistics constraints, a final sub-group of 67 women and girls were assessed clinically for FGS (Figure 1). Thus, within this sub-group, after questioning (questionnaire), consenting participants underwent gynecological examination by colposcopy with photo documentation by a trained gynecologist and midwife, with previous experience in diagnosing FGS. All participants were recruited and screened within the community, mostly in their homes or a 'safe' house prescribed by the women themselves, or the village leader.

Figure 1: Study participant selection criteria and numbers with diagnostic methods flow

After UGS assessment, for girls and women older than 13, a structured questionnaire (see Supplementary File 1) with FGS related symptoms[28], sexual and reproductive health, and socio-demographic questions, was administered privately in a one-to-one format. On average interviews were completed during 35 minutes and were conducted after the urine was collected from each study participant. Participants responded to the structured questionnaire and were prompted to discuss further on related symptoms if they wished to share.

Sexual and reproductive health related questions included: sexual activeness, (with age of first encounter or age at marriage), number of children, age of last child, any miscarriage, menstrual irregularities or abnormalities, abdominal pain, coital pain, and vaginal itches with abnormal discharges. Demographic questions asked included: age, level of formal or informal schooling achieved, water contact activities, and income generating activities. Most females encountered were married by age14, which helped guide the minimum age for the study, in terms of in deciphering a general baseline for assessing girls for FGS (through general sexual health related questions, and invasive gynecological examination) for FGS. Also, age at marriage was used to determine/suggest sub-fertility amongst participants as the age of first child, last child and presence or absence of children was deciphered from the number of years in marriage (or being sexually active)[28, 42]. To better explore age-related profiles, three age groups were formed around these context specific sexual and reproductive health characteristics: adolescence (14-19), young adults (20-35) and older adults (36+).

Parasitological and Gynecological Examinations

Dipstick diagnosis of microscopic haematuria[43], and urine syringe filtration technique with microscopic-based poly-carbonate filter examination for urinary eggs, were used on a single urine sample for standard UGS detection within this study. At least 10 ml of urine was collected and observed for macrohaematuria, tested for microhaematuria and proteinuria with reagent strips (Siemens Multistix

10 SG), then analyzed for *S. haematobuim* eggs, at the local health center laboratory on the same day of collection. Microscopy for visualization of schistosome eggs was performed by x100 using a light compound and stained with Lugol's iodine. A urine sample was deemed positive for UGS on the presence of haematuria[44] with at least one terminal-spined ovum seen[45], and the number of ova reported as per ≥50 (high intensity) or < 50 (low intensity)[46]. Next, consenting eligible girls and women were examined by clinical colposcopy with photo-documentation, using a hand held colposcope (EVA COLPO, Mobile ODT). The obtained images were cross-checked against the WHO FGS pocket atlas[2] to record key sequelae. These were then saved in a coded database for the internal validation through blinded evaluation of cervical images from photo-colposcopy by external team members, after the cross examination with the WHO Pocket atlas. A minimal clinical indication for FGS was determined upon the presence of sandy patches, abnormal blood vessels and/or sandy patches on homogenous yellow areas, in line with the WHO FGS pocket atlas coding[2] after cross verification by external team members

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Statistical Analysis

All numerical data on females examined were extracted from the main database in Excel, and imported into the R (version 4.0.2) software for statistical analyses. In univariate analysis, frequencies and proportions were reported for socio-demographic, syndromic and clinical variables. In bivariate analysis, Pearson's chi-squared tests were used to test the dependence of socio-demographic, clinical and syndromic reproductive health related independent variables against the dependent variables FGS and UGS. To further highlight such dependence, univariate logistic regression analyses was used, with the results presented in the form of unadjusted odds ratios. To identify most relevant variables amongst the reproductive health related independent variables associated to each of UGS and FGS, multivariate logistic regressions analyses were used, with the results presented in the form of adjusted odds ratios (AOR), alongside 95% confidence intervals (CI) and *p*-values based on the Wald's Test. To fit the models, only factors significantly related to the outcomes at a 25% level of significance in the univariate models were included. Multicollinearity between independent variables in the initial multivariate

models were evaluated using the `vif` function in the `car R` package and our knowledge on how the variables were measured. The `step` function in the `R` package `stats` was applied to the resulting multivariate models after correcting for multicollinearity to select the "best" fitting model. The global significance of variables in the final models were evaluated based on analysis of deviance tables using the `anova` function in the `stats R` package. In all, the level of significance was set at *p*-value <0.05.

Results

A. General participant characteristics

A total sample population of 304 females were met, aged from 5 to 69 years old (192 of reproductive age, >13 and <70, with mean±SD age of 28 ±12.7). Also, 88.16% of participants were dependent on, and lived within a proximity of ≤200m to the Mape lake (Island communities), and the remaining 11.82% came from Mainland communities, which were further from the lake (>400m), having alternative water sources (wells and stand taps), and involved in farming alone without fishing activities. Furthermore, 28.29% showed proteinuria, and a 50.0% prevalence (152) was recorded for microhematuria, with a specificity and sensitivity of 74.5% (95% CI: 67.1 – 80.8) and 74.8% (95% CI: 67.4 – 81.1) respectively. The Geometric Mean Egg (GME) count was 33.1 (Range: 2 – 1220) among which 36.2% had heavy (≥ 50 eggs/10ml of urine) infection while 63.8% had light (> 50 eggs/10ml of urine) infection. Macrohematuria was strongly related to egg density categories ($\chi 2 = 17.7$; $P < 0.001$), where cases of macrohematuria were directly related to heavy egg load (93.2%). Information related to sub fertility/infertility was captured based on age at marriage, number of children and the age of last child, with more than half of the study population reporting not having received treatment with praziquantel in more than a year (see Table 1). Reported sexual and reproductive health syndromes showed lower miscarriages (58.89%), abdominal pain (56.95%), lower back pain (44.59%), coital pain (45.98%), coital bleeding (37.93), vaginal itches (68%), abnormal vaginal discharge (42.6%) and menstrual irregularities (47.74%) to be comparatively higher amongst participants, compared to and stress incontinence (19.47) (see Table 1).

Table 1: General characteristics of all study participants (Sociodemographic, syndromic, clinical)

Variable	Category	Number of Women	Percentage
1. Demographic			
Age (groups)	0_<14	111	36.51
	1[14-19]	62	20.39
	2[20-35]	83	27.3
	36+	48	15.79
Age at marriage	13-15	71	39.89
	15-17	88	49.44
	18+	19	10.67
No of Children	0	44	24.31
	1[1-3]	72	39.78
	2[4-6]	37	20.44
	7+	28	15.47
Age of last child	0+	10	7.69
	1[1-3]	67	51.54
	2[4-6]	15	11.54
	7+	38	29.23
Treatment with praziquantel	< 12 months	1	0.3
	> 12 months	292	96.1
	Never	11	3.6
Economic Activity	Fishing (with/without farming)	211	87.5
	Farming (without fishing)	30	12.4
Proximity to lake	<200m	268	88.16
	>400m	36	11.84
2. Syndromic			
Lower Abdominal Pain	Yes	127	56.95
Coital Pain	Yes	80	45.98
Coital bleeding	Yes	66	37.93
Vaginal Itches	Yes	153	68
Vaginal Discharge	Yes	90	42.06
External genital Itch	Yes	86	41.75
Lower back Pain	Yes	99	44.59
Stress Incontinence	Yes	44	19.47
Menstrual Irregularities	Yes	95	47.74
Fertility	Sub fertility (marriage age + youngest child= 4+)	158	88.8%
	Infertility (marriage age + no of children=o)	20	11.2%
Miscarriages	0	74	41.11
	1+	106	58.89
3. Clinical			
Parasitemia	0	141	46.38
	1[1-50]	104	34.21
	50+	59	19.41
Hematuria	+	19	6.25
Microhaematuria	+	152	50
Proteinuria	+	86	28.29

1. UGS Characteristics amongst sample population

Table 2 presents the relationship between UGS as a dependent factor and each of the sociodemographic and reported reproductive health characteristics based on chi-square tests of independence and univariate logistic regression. The results indicate that the chances of UGS infection amongst women who lived more than 400m from the lake was 0.36 (95% CI: 0.17-0.72) times that of women who lived less than

200m to the lake, implying that significant odds of being infected with UGS was seen with closer lake proximity. A significant decrease in chances of infection with urogenital schistosomiasis was observed with increasing age. Relative to girls <14 years, girls between 14-19 years had a 0.46 (95% CI: 0.22-0.95) odds of having UGS, as opposed to 0.29 (95% CI: 0.15-0.54) odds for adults ranging from 20-35 years, and 0.09 (95% CI: 0.04-0.19) odds for women older than 35 years. All reported reproductive health syndromes showed significant relationship with UGS infection, except for stress incontinence (UOR 1.72 [95% CI: 0.87-3.54] p= 0.1287). In effect, women with lower abdominal pain, coital pain, vaginal itch, menstrual irregularity, and coital bleeding showed significantly higher odds (Table 2) of infection with UGS.

Table 2: Relations between UGS and each socio-demographic and syndromic variable in the study sample

			Chi2 Test of Independence			Univariate logistic regression			
Variables	**Category**	**N**	**UGS – n (%)**	**UGS + n (%)**	**P-value**	**Unadjusted OR (95% C.I.)**			**P value**
Age group	<14	111	20 (18.2)	91 (46.9)		1			
	[14-19]	62	20 (18.2)	42 (21.6)		0.46	(0.22,	0.95)	0.0352
	[20-35]	83	36 (32.7)	47 (24.2)		0.29	(0.15,	0.54)	0.0002
	36+	48	34 (30.9)	14 (7.2)	0	0.09	(0.04,	0.19)	0
No of Children	0	44	15 (18.1)	29 (29.6)		1			
	[1-3]	72	33 (39.8)	39 (39.8)		0.61	(0.28,	1.32)	0.2143
	[4-6]	37	16 (19.3)	21 (21.4)		0.68	(0.27,	1.67)	0.3994
	7+	28	19 (22.9)	9 (9.2)	0.0462	0.25	(0.09,	0.66)	0.0063
Age of Last Child	0+	10	4 (6)	6 (9.5)		1			
	[1-3]	67	33 (49.3)	34 (54)		0.69	(0.16,	2.62)	0.5863
	[4-6]	15	4 (6)	11 (17.5)		1.83	(0.33,	10.6)	0.4862
	7+	38	26 (38.8)	12 (19)	0.0323	0.31	(0.07,	1.27)	0.1082
Miscarriages	0	74	41 (48.8)	33 (34.4)		1			
	1	52	19 (22.6)	33 (34.4)		2.16	(1.05,	4.52)	0.0382
	2+	54	24 (28.6)	30 (31.2)	0.1055	1.55	(0.77,	3.17)	0.2216
Lower Abdominal Pain	Yes	127	42 (45.2)	85 (65.4)	0.0039	2.29	(1.33,	3.98)	0.0028
Coital Pain	Yes	80	25 (30.5)	55 (59.8)	0.0001	3.39	(1.82,	6.43)	0.0001
Coital bleeding	Yes	66	19 (23.2)	47 (51.1)	0.0002	3.46	(1.82,	6.79)	0.0002
Vaginal Itches	Yes	153	51 (53.7)	102 (78.5)	0.0001	3.14	(1.77,	5.67)	0.0001
Abnormal Vaginal Discharge	Yes	90	27 (29)	63 (52.1)	0.0008	2.66	(1.51,	4.76)	0.0008
Lower Back Pain	Yes	99	34 (36.6)	65 (50.4)	0.0551	1.76	(1.03,	3.06)	0.0416
Stress Incontinence	Yes	44	14 (14.7)	30 (22.9)	0.1729	1.72	(0.87,	3.54)	0.1287
Genital Itches	Yes	86	26 (28.6)	60 (52.2)	0.0007	2.73	(1.53,	4.94)	0.0008
Menstrual Irregularity	Yes	95	29 (33)	66 (59.5)	0.0002	2.98	(1.68,	5.4)	0.0002
Proximity to lake	<20m	268	89 (80.9)	179 (92.3)		1			
	>200m	36	21 (19.1)	15 (7.7)	0.0051	0.36	(0.17,	0.72)	0.0042

Multivariate Logistic Regression Model for Reporting Sexual and Reproductive Health (SRH) Risk Factors related to UGS

After including all variables significantly related to UGS at a 25% level in a multivariate model, multicollinearity issues were suspected between lower abdominal pain and lower back pain; and external

genital itch and vaginal itches. However, considering genital itch responses were most often related to vaginal itch or misreported by respondents due to their literal similarity in Pidgin English or Fulbe used during questioning, we resorted to keeping only Vaginal Itches in the model. Similarly for lower back pain and lower abdominal pain because of the similarity in responses, but with a more comprehensive responding for lower abdominal pain, lower back pain was removed. The resulting "best" fitting model included Age group, Lower abdominal pain and coital pain as the most significant sexual and reproductive health risk factors for UGS (Table 3). In this result, we also observed a decreasing trend in UGS infection with increasing age. Also, the odds of infection in women with lower abdominal pain was 6.42 (95% CI: 2.85 - 15.68) times that for women without the pain. The odds of infection in women with coital pain was 2.16 (95% CI: 1.05 – 4.46) times that for women without the pain.

Table 3: Possible risk factors for UGS amongst the socio-demographic and SRH included in the study. A multivariate logistic regression model on the effects of sexual and reproductive health factors significantly related to UGS infection.

SRH Indicator	Category	Adjusted OR (95% C.I.)	P value
Age group	[14-19]	1.0	
	20-35]	0.28 (0.10, 0.70)	0.0087
	36+	0.11 (0.04, 0.31)	0.0001
Lower Abdominal Pain	No	1.0	
	Yes	6.42 (2.85, 15.68)	0.0000
Coital Pain	No	1.0	
	Yes	2.16 (1.05, 4.46)	0.0362

2. **FGS Characteristics amongst study participants (Sub group)**

Of the total number of participants examined for FGS after UGS (n=67), 40 were confirmed to have ova-patent UGS, and 34, for FGS upon the presence of homogenous yellow sandy patches, grainy sandy patches, and abnormal blood vessels (Figure 2). Related reproductive health syndromes (as reported in UGS), similarly, were all found to have some association ($P < 0.05$) with FGS manifestation amongst females (Table 4), except for stress incontinence. Of import amongst these, menstrual irregularities or abnormality (collected as irregular, painful or ceased menstruation), more so than found with UGS, was seen to have 7.9 times higher odds of affecting women with FGS than women without FGS (Table 4).

Contrarily to UGS, back pain was seen to significantly affect women with FGS manifestations than was the case with UGS. Similarly, odds of having FGS manifestations were seen to descend with age (Table 4), unlike UGS which was significant with ascending age. Lower abdominal pain, menstrual irregularity and lower back pain showed the highest odds of manifesting amongst women positive for FGS.

Figure 2: Imagery of FGS pathology of the cervix with reported lesions (magnification of x4)

A) 1-rubbery papule, 2-abnormal blood vessel, 3- homogeneous sandy patch (30 year old woman, +UGS, +lower abdominal pain, +Menstrual irregularity) ; **B**) 1,2- grainy sandy patches (45 year old woman, -UGS, +lower abdominal pain ; +Menstrual irregularity)

Table 4: Relations between FGS and socio-demographic and syndromic variables in the sub group of girls and women diagnosed for FGS

			Chi2 Test of Independence			Univariate logistic regression			
Variable	**Category**	**N**	**FGS – n(%)**	**FGS + n(%)**	**P-value**	**Unadjusted OR (95% C.I.)**			**P value**
Age group	[14-19]	19	15 (45.5)	4 (11.8)		1			
	[20-35]	29	11 (33.3)	18 (52.9)		6.14	(1.73,	26.1)	0.0077
	36+	19	7 (21.2)	12 (35.3)	0.0091	6.43	(1.62,	30.35)	0.0116
Age at Marriage	13-15	23	10 (30.3)	13 (38.2)		1			
	15-17	38	22 (66.7)	16 (47.1)		0.56	(0.19,	1.58)	0.2765
	18+	6	1 (3)	5 (14.7)	0.1286	3.85	(0.51,	79.99)	0.2510
No of Children	0	16	12 (36.4)	4 (11.8)		1			
	[1-3]	22	12 (36.4)	10 (29.4)		2.5	(0.64,	11.23)	0.2024
	[4-6]	15	4 (12.1)	11 (32.4)		8.25	(1.79,	46.95)	0.0102
	7+	14	5 (15.2)	9 (26.5)	0.0363	5.4	(1.19,	28.98)	0.0357
Age of Last Child	0+	1	1 (4.8)	0 (0)		1			
	[1-3]	27	14 (66.7)	13 (46.4)		Inf	(0,	Inf)	0.9965
	[4-6]	4	0 (0)	4 (14.3)		Inf	(0,	Inf)	0.9937
	7+	17	6 (28.6)	11 (39.3)	0.1199	Inf	(0,	Inf)	0.9963
Miscarriages	0	26	18 (54.5)	8 (23.5)		1			
	1	22	8 (24.2)	14 (41.2)		3.94	(1.22,	13.78)	0.0256
	2+	19	7 (21.2)	12 (35.3)	0.0362	3.86	(1.14,	14.19)	0.0343
Lower Abdominal Pain	Yes	47	15 (45.5)	32 (94.1)	0	19.2	(4.74,	131.08)	0.0003
Coital Pain	Yes	32	10 (30.3)	22 (64.7)	0.0071	4.22	(1.55,	12.16)	0.0058
Coital bleeding	Yes	29	8 (24.2)	21 (61.8)	0.0029	5.05	(1.82,	15.19)	0.0026
Vaginal Itches	Yes	49	18 (54.5)	31 (91.2)	0.0009	8.61	(2.44,	40.95)	0.0021
Vaginal Discharge	Yes	32	9 (27.3)	23 (67.6)	0.0014	5.58	(2.01,	16.67)	0.0013
Back Pain	Yes	41	12 (36.4)	29 (85.3)	0	10.15	(3.31,	36.45)	0.0001
Stress Incontinence	Yes	10	0 (0)	10 (29.4)	0.0009	Inf	(0,	Inf)	0.9927
Genital Itch	Yes	32	9 (27.3)	23 (67.6)	0.0014	5.58	(2.01,	16.67)	0.0013

Menstrual irregularities	Yes	34	9 (27.3)	25 (73.5)	0.0002	7.41	(2.61,	23)	0.0003
Proximity	<20m	60	30 (90.9)	30 (88.2)	1	1			
	>200m	7	3 (9.1)	4 (11.8)	1	1.33	(0.27,	7.25)	0.7212

Multivariate Logistic Regression Model for Reporting Sexual and Reproductive Health (SRH) Risk Factors related to FGS

Similar to UGS, a multivariate model was constructed with all variables significantly related to FGS at a 25% level. As well, multicollinearity checks revealed lower back pain and genital itch (for same reasons) with the variables age group, coital pain, vaginal itches and lower abdominal pain (Table 5) retained in the "best" fitting model.

Table 5: Possible risk factors amongst SRH for FGS. A multivariate logistic regression model on the effects of FGS infection on sexual and reproductive health factors.

SRH Indicator	Category	Adjusted OR (95% C.I.)	P value
Age group	[14-19]		
	[20-35]	20.15 (2.92, 240.94)	0.0061
	36+	41.29 (4.16, 946.69)	0.0054
Coital Pain	No	1.0	
	Yes	10.44 (2.12, 90.91)	0.0105
Vaginal Itches	No	1.0	
	Yes	12.50 (1.92, 128.77)	0.0151
Lower Abdominal Pain	No	1.0	
	Yes	28.80 (3.36, 578.24)	0.0081

3. UGS, FGS and associations with reproductive health characteristics

Age, number of children, age of last child, menstrual abnormality, miscarriages, and lower abdominal pain were identified as possible reproductive health factors associated with *S. haematobium* infection, and were used within this study. Generally, both FGS and UGS were not significantly (*P*-value >0.05) related to number of children, age of last child and miscarriages. In multivariate logistic regression models, after selection of the best fitting models, the results show that the most significant risk factors for UGS are age group, lower abdominal pain and coital pain (Table 4), whereas age-group and lower abdominal pain, coital pain and vaginal itches were identified as the most significant risk factors for FGS (Table 5).Chances of FGS manifestations amongst women with lower abdominal pain was AOR 9.5(95% CI:1.7-81.8) times that of women without the pain (Table 5). Analysis of deviance tables for

both best fitting models (FGS and UGS), with *p*-values based on likelihood ratio tests are reported in Supplementary File 2.

Discussion

Our study, given our application of portable colposcopy, is the first formal attempt to document the pathology of FGS in a primary care setting in Cameroon. Elsewhere, the clinical pathology of FGS has been described resulting from the complex inflammatory responses to antigens released by adult worms and viable eggs[4, 11], which persists until sometime after adult worms are stopped egg-laying or are destroyed by praziquantel[21]. Thereafter, various signs and symptoms may present months or even years after treatment[20, 37]. Understanding the risks and associations of these UGS and FGS, especially within different contexts of women's health[36, 47], sheds greater light on the disease epidemiology, which could foster improved and coordinated control measures both locally and nationally[36]. Furthermore, precisely documenting existing associations between both FGS and UGS could clarify further the need for precision mapping of schistosomiasis in endemic regions, for formulating a better targeted integrated response[43]. Though a non-significant association was observed between egg intensity in urine and FGS from the onset of this study (Table 2), parasitemia association has been shown to be misleading[5] from several other studies and reports on FGS, particularly when only a single urine sample is examined which is usually the case for population-based surveillance[4]. Considering this, questionnaire (for symptoms)[9, 18], as well as visual examination of cervix and vaginal walls by colposcopy[15, 48], offers an added strength to single sample urinalysis for detection of FGS, as carried out in this study, and several others[9, 15]. The possibility of the presence of FGS in UGS populations has been often raised[6, 18],with projections of about 360 million girls and women possibly infected with UGS[12], but today it is thought that at least 56 million adolescent girls and women are suffering from FGS[12, 14]. Our results maybe show an even higher rate of FGS infection amongst the UGS infected population with an approximate FGS/UGS ratio of 34/40.

From present results, and within the general literature[12, 14], one of such effects noted is an effect on menstrual health. More than half of women within the study who reported poor menstrual health (FGS = 73.5% ; UGS = 54.6%), either as irregular, painful or seized menstruation, were found to either shed eggs in urine (positive for UGS), or were positive for FGS, but without eggs in urine; showing more women positive for FGS reporting abnormal menstruation, than for UGS. This confirms recent analysis[14, 28] and suggests strong linkages between menstrual health management and FGS[12, 14], an under researched area. This can be credited to the fact that symptoms perhaps diminished after a while with UGS (maybe as a result of treatment in mass drug administration campaigns), but later resurface with more chronic sequelae of FGS[14], and with more dire symptoms and negative impact on mental health[14, 28]. In our study context, post-menarche females already faced a substantial challenge with limited access to hygienic material and information on menstrual health management, typically relying on self-made clothes and absorbent plant leaves during menstruation, due to lack of finances or general knowledge.

Still related to FGS and menstrual health, narratives from a previous study[28] which used qualitative probing showed women having manifestations of FGS and not shedding eggs in urine, gave a history of having lived in their earlier years in heavily infested *S. haematobium* foci, which explained their later manifestation of FGS symptoms, even after having moved away to a less infested area, with more than 90% limit in fresh water contact[28]. This as well relates to this study, where compared to UGS, lake proximity was seen to be not very significant to disease manifestation (Table 5), same like egg shedding, still pointing to early-in-life infection and later chronicity. Significant difference in menstrual abnormalities amongst UGS positive women [n=22(56.4)] and UGS negative women [n=12 (44.4)], alerts to future chronicity of FGS after infection with UGS, especially if not managed with more readily available praziquantel treatment(s)[37, 49].

On its own, lower abdominal pain observed significant association (in adjusted and unadjusted regression models) in both UGS and FGS infections. The chances of having lower abdominal pain was significantly higher in females with either FGS (94.1%) or UGS (84.2%). Similarly with coital pain and vaginal itches, these reported as key indicators for UGS and FGS, directing early diagnosis of UGS and

future FGS in endemic communities, promoting the verticalization of control strategies for both diseases.

Another trend observed in this study is that intensity of infection or egg patent-prevalence (for UGS) reduces while chronic disease or morbidity for FGS increases as women age. Since women aged (36+), chances of FGS after infection with UGS increased significantly (AOR 6.43,95% C.I 1.62-30.35, P=0.0091), similarly reported in other studies in different geographical locations[4, 11, 50, 51] and recently in this area[28]; emphasizing on the level of present intensity of infection for UGS, and possible future occurrence of FGS[11, 51]. UGS at a younger age will in some cases manifest into FGS when the female is older[11], causing more intense gynecological symptoms and effects. This offers a possible guiding tool for better control policies, related to early diagnosis and treatment[36, 52]. This surpasses need alone for school-based MDAs[24], but considers and encourages individual therapy in different contexts for FGS (and MGS)[4].

Although only a few amongst the extensive list of reproductive health determinants [54] were identified in this study to be statistically significant, where mostly reported symptoms were collected, clinical and biological examinations carried out, enabled confirmation of how future self-reported symptoms with UGS and FGS might be best used[28]. These results support the advocated need for availability of praziquantel in lowest level (Health Areas and community) of health care for individual therapy[51], as well as treatment from a younger age[12, 24, 36, 49] buoyed with the recent development of pediatric praziquantel[53].

Study Limitations

Though described as gold standard[45], active UGS was only detected through observation of eggs in urine sediments by microscopic-based poly-carbonate filter examination, as well as recommended dipstick assays for urinary haematuria detection. Alternative molecular assays molecular assays such as polymerase chain reaction (PCR) for schistosome detection in human serum and urine samples, were not considered for added sensitivity for UGS and FGS (in vaginal lavage analysis)[54]. Though recommended[18, 55], only visual examination through inspection for lesions on the cervix, the fornices,

and the vaginal walls with a colposcope[2, 48] and screening with questionnaires was considered in the detection of FGS in this study. Lastly, the sample population for FGS detection (n=67) was limited to girls older than age 13, though other reports have shown pre-puberty girls younger than 10 could manifest gynecological damages as a result of infection with urogenital schistosomiasis[11]. In this study, examination for this group of girls could be limited only to questionnaire, for ethical purposes.

Conclusion

Whilst millions of women in Cameroon have UGS, its epidemiological connection with FGS is not fully appreciated, which creates an unfortunate knowledge holdup for effective control at the public health level. In our chosen study location, which is broadly typical for endemic areas of UGS in Cameroon[18, 29, 31, 35], strong epidemiological associations between UGS and FGS were found against certain key sexual and reproductive determinants: age, lower abdominal pain and menstrual health. This formative knowledge could be utilized to tackle and ultimately prevent FGS, with a more targeted integrated control for UGS in Cameroon and elsewhere in endemics areas for UGS globally. This study further adds detailed insight into the connection of FGS and UGS within primary care in endemic communities, denoting those with cardinal symptomologies more explicitly for scalable detection and targeted control of FGS within UGS endemic areas.

Supporting Files

Supplementary File 1.docx : Structured questionnaire

Supplementary File 2.docx: Deviance Table

Declarations

- **Authors' contributions**

MCM and JRS conceptualized the study and planned the methodology; AEN,VG, MCM, carried out field investigation; MCM, FNB, JRS, ASO, AEN, analyzed and interpreted the data for this manuscript; MCM acquired funding for study and wrote the original draft of the manuscript; JRS supervised the study and was a major contributor in the conceptualization and writing of the manuscript; AEN,

coordinated field activities within the Malanteoun Health District; AEN, FNB, VG, ASO, reviewed and edited the manuscript. All authors approved the final version of the paper before submission.

- **Competing interests**

The authors declare that they have no competing interests.

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- **Data Sharing Statement**

All data generated or analysed during this study are included in this published article [and its supplementary files].

- **Acknowledgements**

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- **Consent for publication**

Written informed consent for publication of clinical details and/or clinical images was obtained from the patients and parents/guardians where needed.

References

1. Søfteland S, Sebitloane MH, Taylor M, Roald BB, Holmen S, Galappaththi-Arachchige HN, et al. A systematic review of handheld tools in lieu of colposcopy for cervical neoplasia and female genital schistosomiasis. International Journal of Gynecology & Obstetrics. 2021;153(2):190-9.
2. WHO. Female Genital Schistosomiasis: A Pocket Atlas for Clinical Health-Care Professionals Geneva: WHO Press; 2015 [Available from: https://www.who.int/publications/i/item/9789241509299.
3. Botelho MC, Machado JC, Brindley PJ, Correia da Costa JM. Targeting molecular signaling pathways of Schistosoma haemotobium infection in bladder cancer. Virulence. 2011;2(4):267-79.

4. Kjetland E, Leutscher P, Ndhlovu P. A review of female genital schistosomiasis. Trends in Parasitology. 2012;28(2):58-65.
5. Poggensee G, Kiwelu I, Saria M, Richter J, Krantz I, Feldmeier H. Schistosomiasis of the lower reproductive tract without egg excretion in urine. Am J Trop Med Hyg. 1998;59(5):782-3.
6. Christinet V, Lazdins-Helds J, Stothard J, Reinhard-Rupp J. Female genital schistosomiasis (FGS): from case reports to a call for concerted action against this neglected gynaecological disease. International Journal for Parasitology. 2016;46(7):395-404.
7. Freer JB, Bourke CD, Durhuus GH, Kjetland EF, Prendergast AJ. Schistosomiasis in the first 1000 days. The Lancet Infectious Diseases. 2018;18(6):e193-e203.
8. Shams M, Khazaei S, Ghasemi E, Nazari N, Javanmardi E, Majidiani H, et al. Prevalence of urinary schistosomiasis in women: a systematic review and meta-analysis of recently published literature (2016–2020). Tropical Medicine and Health. 2022;50(1):12.
9. Ekpo U, Odeyemi O, Sam-Wobo S, Onunkwor O, Mogaji H, Oluwole A, et al. Female genital schistosomiasis (FGS) in Ogun State, Nigeria: a pilot survey on genital symptoms and clinical findings. Parasitology Open. 2017;3:e10.
10. Hotez PJ, Engels D, Gyapong M, Ducker C, Malecela MN. Female Genital Schistosomiasis. New England Journal of Medicine. 2019;381(26):2493-5.
11. Hegertun I, Gundersen S, Kleppa E, Zulu S, Gundersen S, Taylor M, et al. S. haematobium as a common cause of genital morbidity in girls: a cross-sectional study of children in South Africa. PLoS neglected tropical diseases. 2013;7(3):e2104.
12. UNAIDS. 'No more neglect:Female genital schistosomiasis and HIV. www.unaids.org/en/resources/documents/2019/: UNAIDS; 2019.
13. Hotez P. Speaking of Medicine and Health [Internet]. BLOGS P, editor: PLOS BLOGS. 2013. Available from: https://speakingofmedicine.plos.org/2013/05/06/female-genital-schistosomiasis-fgs-sub-saharan-africas-secret-scourge-of-girls-and-women/.
14. Stothard JR, Odiere MR, Phillips-Howard PA. Connecting Female Genital Schistosomiasis and Menstrual Hygiene Initiatives. Trends in Parasitology. 2020;38(5).
15. Bustinduy AL, Randriansolo B, Sturt AS, Kayuni SA, Leustcher PDC, Webster BL, et al. An update on female and male genital schistosomiasis and a call to integrate efforts to escalate diagnosis, treatment and awareness in endemic and non-endemic settings: The time is now. In: Rollinson D, Stothard R, editors. Advances in Parasitology. 115: Academic Press; 2022. p. 1-44.
16. Majangara Karaga R. Concealed urogenital schistosomiasis causing chronic pelvic pain: A case report. Clinical Case Reports. 2021;9(4):1860-4.
17. Stothard J. Female genital schistosomiasis - icebergs of morbidity ahead? Trends in parasitology. 2012;28(5):174-5.
18. Campbell S, Stothard J, O'Halloran F, Sankey D, Durant T, Ombede D, et al. Urogenital schistosomiasis and soil-transmitted helminthiasis (STH) in Cameroon: An epidemiological update at Barombi Mbo and Barombi Kotto crater lakes assessing prospects for intensified control interventions. Infect Dis Poverty. 2017;6(1):49-.
19. King C. Parasites and poverty: the case of schistosomiasis. Acta Trop. 2010;113(2):95-104.
20. Kjetland EF, Mduluza T, Ndhlovu PD, Gomo E, Gwanzura L, Midzi N, et al. Genital schistosomiasis in women: a clinical 12-month in vivo study following treatment with praziquantel. Trans R Soc Trop Med Hyg. 2006;100(8):740-52.
21. Treatment of Female Genital Schistosomiasis (FGS) With Praziquantel: A Proof-of-Concept Study (NCT04115072) [Internet]. NIH: ClinicalTrials.gov archive. 2020 [cited 31/01/2022].
22. Brindley PJ, Hotez PJ. Break Out: urogenital schistosomiasis and Schistosoma haematobium infection in the post-genomic era. PLoS neglected tropical diseases. 2013;7(3):e1961.
23. Kukula VA, MacPherson EE, Tsey IH, Stothard JR, Theobald S, Gyapong M. A major hurdle in the elimination of urogenital schistosomiasis revealed: Identifying key gaps in knowledge and understanding of female genital schistosomiasis within communities and local health workers. PLoS neglected tropical diseases. 2019;13(3):e0007207.

24. Faust CL, Osakunor DNM, Downs JA, Kayuni S, Stothard JR, Lamberton PHL, et al. Schistosomiasis Control: Leave No Age Group Behind. Trends Parasitol. 2020;36(7):582-91.
25. World Health Organisation. WHO guideline on control and elimination of human schistosomiasis. https://www.who.int/publications/i/item/9789240041608: WHO; 2022. p. 142.
26. SCI Foundation. FAST PACKAGE PROJECT 2021 [Available from: https://schistosomiasiscontrolinitiative.org/projects/fast-research-project
27. Ndassi VD, Anchang-Kimbi JK, Sumbele IUN, Ngufor LA, Nadege K, Kimbi HK. The epidemiological status of urogenital schistosomiasis among reproductive aged individuals in the Tiko Health Area- a semi-urban setting in the Mount Cameroon area. PLOS Neglected Tropical Diseases. 2021;15(1):e0008978.
28. Masong MC, Wepnje GB, Marlene NT, Gamba V, Mengue M-T, Kouokam E, et al. Female Genital Schistosomiasis (FGS) in Cameroon: A formative epidemiological and socioeconomic investigation in eleven rural fishing communities. PLOS Global Public Health. 2021;1(10):e0000007.
29. TchuentÉ LAT, N'Goran EK. Schistosomiasis and soil-transmitted helminthiasis control in Cameroon and Côte d'Ivoire: implementing control on a limited budget. Camnbridge core. 2009;136(13):1739-45.
30. National Program for the control of Schistosomiaisis and intestinal helminthiases MoPHC. Towards elimination of Schistosomiasis and Soil-transmitted Helminthiasis and in Cameroon: A road map for paradigm shift 2021-2030. MINSANTE, Yaoundé: MINSANTE; 2022.
31. National Program for the control of Schistosomiaisis and intestinal helminthiases. Progress Report Cameroon 2013-2019. Yaoundé: MINSANTE; 2019.
32. World Health Organization. Global update on implementation of preventive chemotherapy against neglected tropical diseases in 2018. Weekly Epidemiological Record 2019;94(38):425-38.
33. Crompton DWT, World Health Organization. Preventive chemotherapy in human helminthiasis : coordinated use of anthelminthic drugs in control interventions : a manual for health professionals and programme managers. Geneva: World Health Organization; 2006.
34. Makia C, Ozano K, Tagne M, Tchoffo M, Ngang S, Thomson R, et al. Achieving equity in UHC interventions: who is left behind by neglected tropical disease programmes in Cameroon? Glob Health Action. 2021;14(1):1886457-.
35. Njunda A, Ndzi E, Assob J, Kamga H, Kwenti E. Prevalence and factors associated with urogenital schistosomiasis among primary school children in barrage, Magba sub-division of Cameroon. BMC Public Health. 2017;17(1):618.
36. WHO. Deworming adolescent girls and women of reproductive age. Policy Brief [press release]. Geneva: WHO2022.
37. Nour NM. Schistosomiasis: health effects on women. Rev Obstet Gynecol. 2010;3(1):28-32.
38. MINSANTE. Schistosomiasis distribution in Malanteoun Health District NTDmaps.org: MINSANTE; 2018 [Available from: https://ntdmaps.org/.
39. National Institute of Statistics Cameroon. Socio-economic statistics of Cameroon, 2015 Cameroon2004-2014 [Available from: https://cameroon.opendataforafrica.org/SESC2015/socio-economic-statistics-of-cameroon-2015.
40. Keptcheu T, Khan P, Gustave L, Gangue T. Some Haematological Parameters among Urinary Schistosomiasis-Malaria Coinfected Children in Suburb of Malentouen Health District, West Region Cameroon. International Journal of TROPICAL DISEASE & Health,. 2020;41(7):34-44.
41. Daniels W. Biostastistics: A foundation for analysis in the health sciences. New York: Wiley & sons; 1999.
42. Beekhuizen Hv, Sharma S. Subfertility. In: Unkels HvBaR, editor. A Textbook of Gynecology for Less-Resourced Locations. London NW3 3AY, UK: Global Library of Women's Medicine , Sapiens Publishing; 2012. p. 170.
43. Colley DG, Bustinduy AL, Secor WE, King CH. Human schistosomiasis. Lancet. 2014;383(9936):2253-64.

44. King CH, Bertsch D. Meta-analysis of urine heme dipstick diagnosis of Schistosoma haematobium infection, including low-prevalence and previously-treated populations. PLoS neglected tropical diseases. 2013;7(9):e2431.
45. World Health Organisation. Schistosomiasis WHO: WHO; 2022 [cited 2022. Available from: https://www.who.int/news-room/fact-sheets/detail/schistosomiasis.
46. WHO. Prevention and Control of Schistosomiasis and Soil Transmitted Helminths Geneva: WHO; 2002 [33/63]. Available from: http://apps.who.int/iris/bitstream/handle/10665/42588/WHO_TRS_912.pdf;jsessionid=297C20DDFCBFFF9F9AAE9DF120C0F834?sequence=1.
47. World Health Oganization. Regional Office for the Western Pacific. People Centered Health care: A policy framework. 2007.
48. Kjetland EF, Norseth HM, Taylor M, Lillebø K, Kleppa E, Holmen SD, et al. Classification of the lesions observed in female genital schistosomiasis. Int J Gynaecol Obstet. 2014;127(3):227-8.
49. Bustinduy AL, Friedman JF, Kjetland EF, Ezeamama AE, Kabatereine NB, Stothard JR, et al. Expanding Praziquantel (PZQ) Access beyond Mass Drug Administration Programs: Paving a Way Forward for a Pediatric PZQ Formulation for Schistosomiasis. PLOS Neglected Tropical Diseases. 2016;10(9):e0004946.
50. Chetty A, Omondi MA, Butters C, Smith KA, Katawa G, Ritter M, et al. Impact of Helminth Infections on Female Reproductive Health and Associated Diseases. Front Immunol. 2020;11:577516.
51. Stothard JR, Stanton, M, Bustinduy, A, Sousa-Figueiredo, J C, Van Dam, GT, Betson, M, et al.,. Diagnostics for schistosomiasis in Africa and Arabia: A review of present options in control and future needs for elimination. Camnbridge core. 2014(141):1947-61.
52. Richardson ST, Franklin AL, Rome ES, Simms-Cendan JS. Global Health: Urogenital Schistosomiasis in the Adolescent Girl. Journal of Pediatric and Adolescent Gynecology. 2016;29(4):326-32.
53. Pediatric Praziquantel Consortuim. Contract manufacturing agreement signed for production of new pediatric treatment for schistosomiasis 2021 [Available from: http//:https://www.pediatricpraziquantelconsortium.org/.
54. Sturt A, Webb E, Phiri C, Mweene T, Chola N, van Dam G, et al. Genital self-sampling compared with cervicovaginal lavage for the diagnosis of female genital schistosomiasis in Zambian women: The BILHIV study. PLOS Neglected Tropical Diseases. 2020;14(7):e0008337.
55. Utzinger J, Becker SL, van Lieshout L, van Dam GJ, Knopp S. New diagnostic tools in schistosomiasis. Clinical Microbiology and Infection. 2015;21(6):529-42.

- **Figure Legends**

Figure1: Study participant selection criteria and numbers with diagnostic methods flow

Figure 2: Imagery of FGS pathology of the cervix with reported lesions (magnification of x4)

A) 1-rubbery papule, 2-abnormal blood vessel, 3- homogeneous sandy patch (30-year-old woman, +UGS, +lower abdominal pain, +Menstrual irregularity); **B**) 1,2- grainy sandy patches (45-year-old woman, -UGS, +lower abdominal pain; +Menstrual irregularity)

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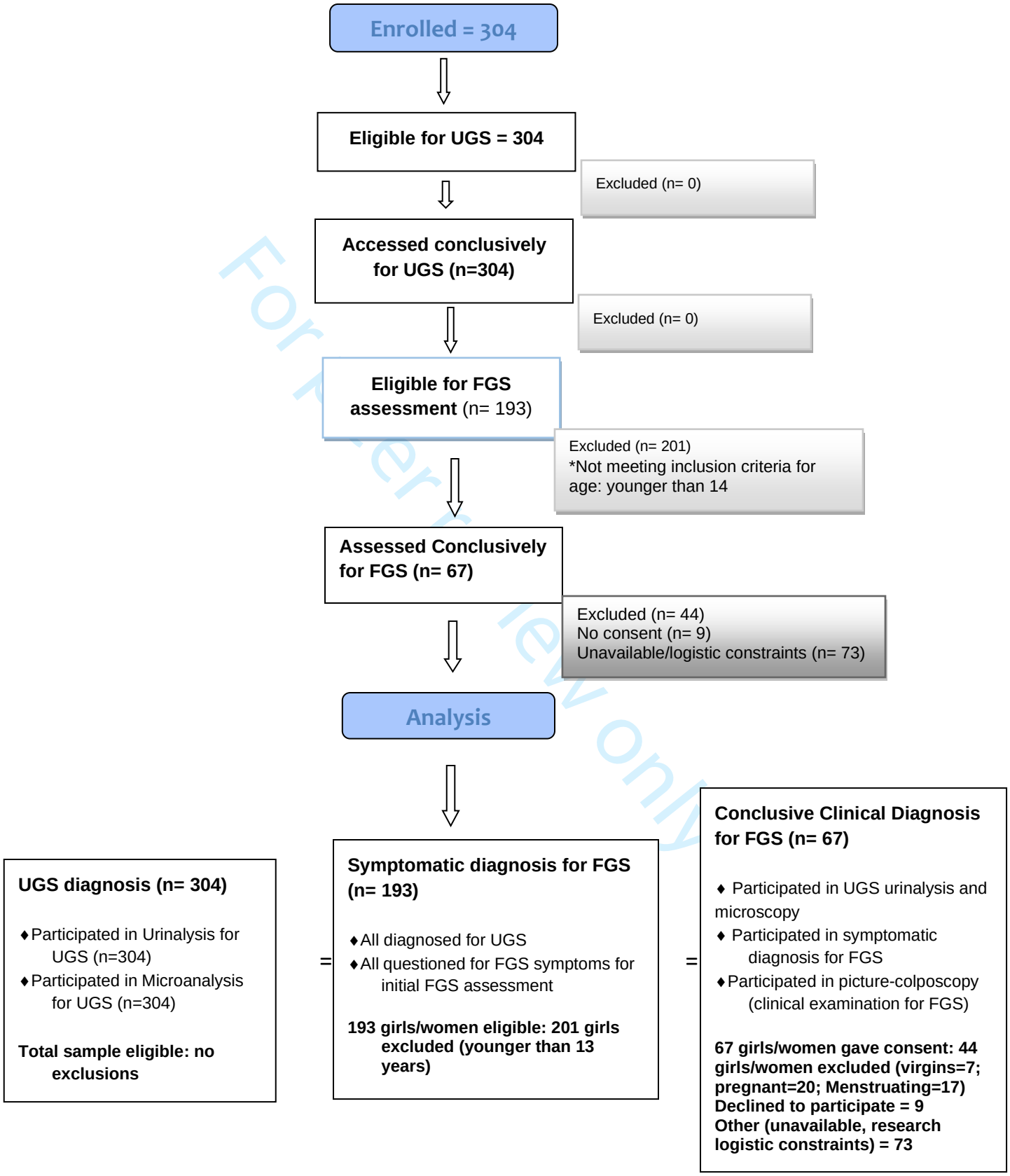
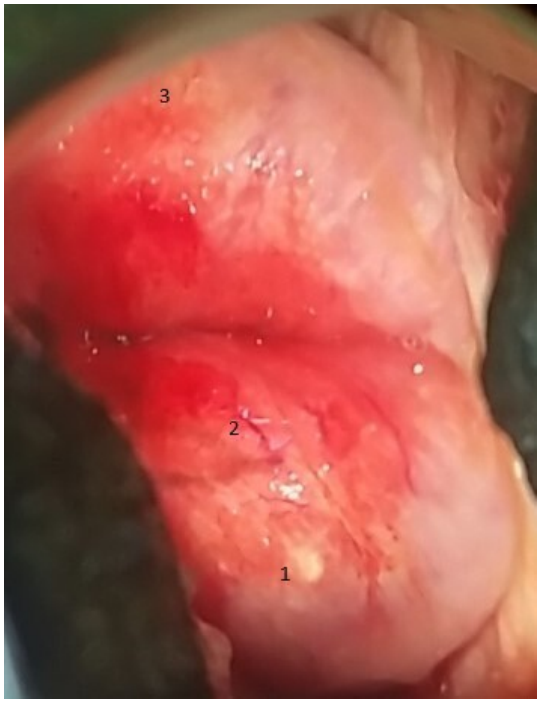
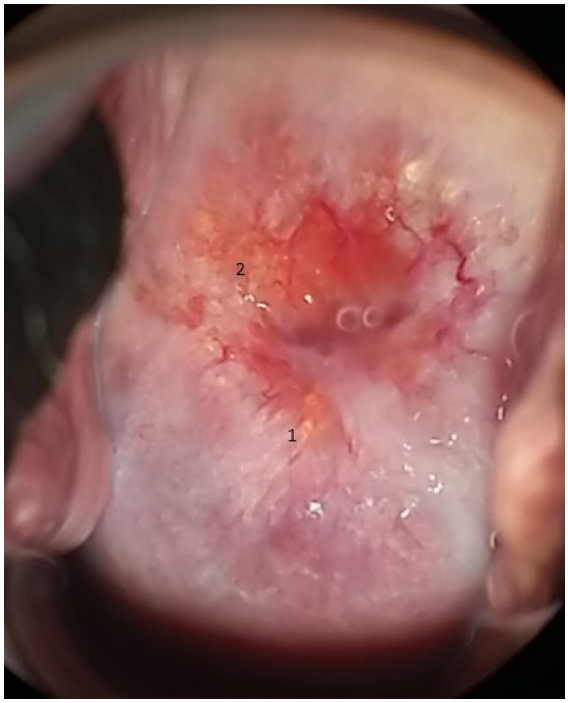
Sampling Flow Diagram



A	B
	

Supplemantary File 1

Close-ended structured questionnaire

A. Close ended structured questionnaire– Administered directly in English with oral translations into Fulbe, Kotoko, Mosgum, and Arab

Name of Community: _____

Age (years): _____

Education: Informal education () Formal education () (specify)_____

Marital Status: Single ( ) Married ( ) Separated ( ) Widowed ( )

No of years having lived in community _____

Previous community _____

Economic activity----------

Residence ---------- (collect coordinates)

Questions on symptoms of urinary tract schistosomiasis; FGS; OR STI

1. Do you see your menses? Yes ( ) No ( )
2. Did you observe/experience your menses within the last two weeks? Yes ( ) No ( ) Does your menses come every month? Regular?
3. Is your menses painful? _____(pain during menstruation – always very painful, sometimes painful, normal) Irregular? _____(every month?, not every month, stopped)
4. Do you have pain in your lower abdomen? When? For how long?
5. Do you have pain when urinating? Yes ( ) No ( )
6. Do you have difficulty in urinating (urine not coming out fluently)? Yes ( ) No ( )
7. Do you have sudden uncontrollable and unexpected urge to urinate and mostly cannot hold it? Even when you cough it comes out? Yes ( ) No ( )
8. Do you see blood in your urine? Yes () No ()
9. (If yes) When did you lastly see blood in your urine? _____Always, sometimes, Once in a while
10. Do you sometimes haveitching in your private part?Yes ( ) No ( )
11. How often do you experience this? Once a while ( ) frequently ( )/ When was the last time?
12. Do you have a feeling of burning within your private part? Yes ( ) No ( )

13. How often do you experience this? Once a while ( ) Frequently ( )

14. Do you sense a swelling/lumps within your private part? Yes ( ) No ( ) No response ( )

15. Do you have any discharge that comes from your vagina? Yes () No () Does it have an ordure? _____ Do you see the colour? Yes ( ) No ( ) What Color is it?White; grey; green/yellow; brown

16. Do you think this is normal? Yes () No() Do not know(). When did you start observing the discharge? Date _____

17. After sexual intercourse do you have a discharge? Yes () No () Is it smelly? Yes () No () Do not know ()

18. After or during sexual intercourse do you have pain?Yes ( ) No ( ) I do not know ( ) ; Do you have a bloody discharge?Yes ( ) No ( ) I do not know ( )

19. Have you had any miscarriages /pregnancies that passed? Yes ( ) No ( )

20. How many? ()

21. Do you have children? Yes() No()

22. What age is your last child? ()

23. Have you visited the clinic to complain about these issues? Yes ( ) No ( )

24. What you used/taken/done to treat any of these problems? _____ (Underline) Hospital or drug store/ local midwife/ traditional medicine/ prayers/ none of the above (what other? Specify)/nothing

Water contact History

1. Where do you fetch your household water? Lake; other source (name) _____
2. Do you fish in the lake? Yes (), No ()
3. Do you bathe in the lake? Yes (), No ()
4. What do you use the lake for? ()_____

Supplementary file 2

Analysis of deviance tables for both best fitting models (FGS and UGS), with *p*-values based on likelihood ratio tests

Variable	Df	Deviance	Resid. Df	Resid. Dev	Pr(>Chi)
UGS					
Age2	2	19.0094	162	208.70	7.450e-05 ***
Lower Abdominal Pain	1	25.6949	161	183.01	3.999e-07 ***
Coital Pain	1	4.4254	160	178.58	0.03541 *
FGS					
Age2	2	9.8057	64	83.061	0.0074253 **
Coital Pain	1	11.3146	63	71.747	0.0007690 ***
Vaginal Itches	1	13.1740	62	58.573	0.0002839 ***
Lower Abdominal Pain	1	10.5961	61	47.976	0.0011333 **

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-6
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	7-10
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	8-9
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	/
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*8-11*
Bias	9	Describe any efforts to address potential sources of bias	/
Study size	10	Explain how the study size was arrived at	7-9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9-10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	7-8
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	/

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	/
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11-13
		(b) Give reasons for non-participation at each stage	7-8
		(c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11-13
		(b) Indicate number of participants with missing data for each variable of interest	/
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	/
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	/
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	/
		Cross-sectional study—Report numbers of outcome events or summary measures	11-13
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9, 12-15
		(*b*) Report category boundaries when continuous variables were categorized	9, 12-15
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	/
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	/
Discussion			
Key results	18	Summarise key results with reference to study objectives	18-20
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	21
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Urogenital Schistosomiasis (UGS) and Female Genital Schistosomiasis (FGS) in Cameroon: An observational assessment of key reproductive health determinants of girls and women in the Matta Health Area

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Title: Urogenital Schistosomiasis (UGS) and Female Genital Schistosomiasis (FGS) in Cameroon: An observational assessment of key reproductive health determinants of girls and women in the Matta Health Area

Authors: Makia Christine Masong[1*], Fesuh Nono Betrand[2], Amabo Elvis Ngwa[3], Victoria A. Gamba[4], Akinola Stephen Oluwole[5], J. Russell Stothard[6]

[1]Department of Social Sciences and Management, Catholic University of Central Africa, Yaoundé, Cameroon

[2]Department of Mathematics and Physical Sciences, National Advanced School of Engineering, University of Yaoundé 1, Cameroon

[3]Malanteoun Health District, Malanteoun, Cameroon

[4]Department of Obstetrics and Gynecology, University of Nairobi, Nairobi, Kenya

[5]Department of Pure and Applied Zoology, Federal University of Agriculture, Abeokuta, Nigeria

[6]Department of Tropical Disease Biology, Liverpool School of Tropical Medicine, Liverpool, L3 5QA, UK

*Corresponding author

Makia Christine Masong

Department of Social Sciences and Management, Catholic University of Central Africa, Yaoundé, Cameroon

Projet MTN/OCEAC

masongbye@yahoo.com

Abstract

Objectives and Setting: Across sub-Saharan Africa, urogenital schistosomiasis (UGS), in particular female genital schistosomiasis (FGS) is a significant waterborne parasitic disease, with its direct burden upon the sexual and reproductive health (SRH) of sufferers infrequently measured. UGS has an established control plan, which in most endemic regions as in Cameroon, still excludes FGS considerations. Highlighting existent associations between UGS and FGS could increase the management of FGS within UGS interventions. This study seeks to identify current associations amongst FGS and UGS with some reproductive health indicators, to provide formative information for better integrated control.

Participants: 304 females aged 5 - 69 years, were all examined for UGS by urine filtration and microscopy. Amongst these, 193 women and girls were eligible for clinical FGS assessment based on age (>13). After selective questioning for FGS symptoms, a sub-group of 67 women and girls consented for clinical examination for FGS using portable colposcopy, with observed sequelae classified according to the WHO FGS pocket atlas.

Outcome: Overall UGS and FGS prevalence was measured, with FGS/UGS related reproductive health symptoms recorded. Associations between FGS and UGS were investigated by univariate and multivariate logistic regression analyses.

Results: Overall UGS prevalence was 63.8% (194/304), where FGS prevalence (sub-group) was 50.7% (34/67). FGS manifestation increased significantly with increasing age, whilst a significant decrease with ascending age was observed for UGS. Lower abdominal pain (LAP) vaginal itches (VI), and coital pain (CP), were identified as the main significant shared symptoms of both FGS and UGS, while LAP with menstrual irregularity (MI) appeared a strong symptomatic indicator for FGS.

Conclusion: LAP, MI, CP and VI are potential SRH indicators that could be exploited in future for targeting of praziquantel provision to FGS sufferers within primary care, complementary with existing Praziquantel distribution for UGS sufferers in *S. haematobuim* endemic areas.

Keywords: *Schistosoma haematobium*, SRH, clinical colposcopy, questionnaires, menstrual health, abdominal pain

Strengths and Limitations of this study

Strength

- This study used clinical colposcopy, which is the recommended diagnostic method for FGS, though not very common within primary health care settings in sub-Saharan Africa.

- Here, questionnaire approach is used to better capture individual experiences of FGS sufferers within endemic areas for UGS.

- Clinical diagnosis of girls younger than 14 (about half of the study participants) was not considered, because of the invasive nature of colposcopy examination, especially as non-invasive clinical diagnostic tools are lacking for examination amongst this age group within low resource schistosomiasis endemic communities.

- Clinical diagnosis for FGS was carried out only on a limited sample

- Assessment for STIs amongst participants are not presented here, whereby such results could complement or clarify FGS diagnosis, considering most sexual and reproductive health related symptoms for urogenital schistosomiasis present as sexually transmitted infections, and can be misdiagnosed.

Introduction

In endemic areas, a definitive diagnosis of urogenital schistosomiasis (UGS) is established by demonstration of viable *Schistosoma (S) haematobium* eggs (≥1) in urine or hematuria[1-3], whilst female genital schistosomiasis (FGS) can be diagnosed visually[4] for *S. haematobium* induced cervical lesions and small fibrotic nodules known as "sandy patches"[5], either with the presence or absence of *S. haematobuim* eggs in urine[4, 6, 7]. Whilst both FGS and UGS are caused by infection with *Schistosoma haematobium*[1, 4, 8, 9] a waterborne blood fluke, each appear to have some unclear epidemiological associations, largely due to insufficient disease surveillance[6, 7, 10-13]. In sub-Saharan Africa where UGS is endemic and can be highly prevalent (>50%)[14, 15], insufficient or infrequent efforts have been undertaken to document FGS specifically[11, 16-18], partly as the clinical skills to do so are lacking and uninformed within primary care[10]. While active UGS does not readily predict FGS[6], since FGS can occur without the direct presence of schistosome eggs in urine (a cardinal diagnostic for UGS)[18, 19], rather FGS often presents with a more chronic time frame where schistosome eggs are trapped within the cervico-vaginal surfaces[6, 20, 21]. For some, these trapped eggs can accumulate from very early on in life[1], with enduring and typically hidden sequelae[20, 22]. Based on several biological determinants such as age[1], the mucosal damage and fibrotic scarring of the vaginal and cervical surfaces from FGS proceeds with increasing duration of UGS[6]; moreover, FGS-specific sequelae maybe slow to resolve upon standard antiparasitic treatment of UGS[23, 24], i.e., single annual administration of praziquantel at 40mg/g as used in public health campaigns[6, 13, 20].

In many parts of Africa where surveillance of UGS is limited[25, 26] and that for FGS largely absent[15, 27], there is a clear need to better understand the epidemiological associations between UGS and FGS[14]. Particularly so, to support earlier diagnosis of cases of FGS, and individualize praziquantel treatment needs (for individual and context specific case management)[15, 28] to better avert their disease progression[15]; as current interventions against UGS do not specifically target adolescent girls or women[23, 29]. This gap in treatment coverage[28] and surveillance[13, 30] also has considerable bearing on progress towards elimination of schistosomiasis transmission within disease endemic communities[29].

In recent years, FGS focused research and public health education[31] has gained traction in certain countries such as Ghana, Tanzania, Madagascar, Nigeria, and Mozambique[8, 9], although other countries such as Cameroon, currently lag behind[32, 33]. Schistosomiasis exists in several regions of Cameroon[34], affecting over 10 million people in rural and urban areas[35]. The country has a national coordinated control plan for fairly early interventions during child-hood years (from 5 – 14 years old)[36], which take advantage of school based intervention platforms[37, 38], and in certain settings, community based interventions, where their at-risk status (people or communities dependent on schistosomiasis endemic water bodies, for main water source) is high[21, 32, 36, 39, 40]. Even with improved (>70%) helminth control amongst children in the last decade [35], some of the adolescent at-risk populations do not always benefit from praziquantel treatment due to existing policy gaps and program intervention challenges [[15, 41, 42].

To address this treatment deficit, capture missed opportunities, and ensure the consideration and apprehension of ensuing FGS manifestations within such already identified sub-groups (young girls and women); with better knowledge on the precise associations between UGS and FGS; future control policies and intervention campaigns can be revised to better target at-risk populations.

Here, we sought to clarify existing associations between FGS and UGS, highlighting cardinal symptomologies for scalable detection and targeted control of FGS within UGS endemic areas. This supports the need for a future integrated approach for control of schistosomiasis and limits the "gap" concerning FGS surveillance within current primary care.

Materials and Methods

Ethics approval and consent to participate

Ethical clearance for this study was provided by the Cameroon National Ethics committee on Human Health Research (Ref N ° 2020/07/1266/CE/CNERSH/SP), with administrative authorizations from both the Regional Delegation of Public Health for the West region of Cameroon (Ref N° 679/L/MINSANTE/SG/DRSPO/CBF), and the district Health Office of the Malanteoun Health District (Ref N° 078/L/MINSANTE/DRSPO/DSMLT). Informed written and oral consent was obtained from

all participants for parasitological and gynecological examinations. For participants <18 years, parents, husbands, or guardian gave informed permission and assent was obtained from the participants. Privacy and confidentiality of medical information were protected during and after the study.

Patient and Public Involvement

We followed inclusive and participative methods to get overall participant and public involvement. Tailored visits for data collection were carried out according to best practices with local engagement of key community members and local health workers.

Study Setting

This study was carried out across a group of girls and women residing in remote communities surrounding the Mape Dam, a known transmission focus for *Schistosoma haematobium*[35, 40] in the Matta Health Area in Cameroon. Most study participants were involved actively in fishing or other household activity that put them in constant contact with the lake water[33]. More than 90% of the population lived less than 200m to infested water source (the Mape Dam), and more than 75% depended fully on the Mape Dam for house-hold water and for an income generating activity (fishing) [13]. The Matta Health Area hosts several remote fishing island communities that surround this man-made water body, and for at least 18 years has witnessed high transmission of *s. haematobium* with prevalence of UGS greater than 50% amongst children[43].

Study Design and Procedures

This cross-sectional study was conducted between December 2020 and June 2021. The total population estimate of the study site was 5,000 [44], where females represented approximately 51.0%. About 54.6% of the population of females were aged 5-69 years. The sample size estimation for this study was based on UGS prevalence (considered as key indicator for the study). With no existing records of UGS prevalence amongst adults within the Matta Health area, a hypothesis of UGS endemicity amongst adults was based on recorded school-age schistosomiasis prevalence (> 41% in the last decade) within the Matta health Area[43, 45]. In this context made up of primarily fishing communities, more than 80% of adults (both male and female) spent long stretches a day in contact with water (for economic -fishing-

or household activity purposes) [37]. Based on this, we assumed UGS prevalence in such communities should be higher amongst women. Hence, we resorted to an estimate of 55% for UGS prevalence in the Matta health area, for our sample size calculation. Considering lake proximity and economic activities, 11 main communities were involved within the Matta Health Area: nine secluded water-locked fishing communities (Islands/fishing camps) with habitations mostly less than 200m from the lake; and two mainland communities (land-locked) with habitation more than 400m from the lake[33].

Following a simple random sampling technique, on the base of attaining a precision rate of 95% with an error margin of 5%, our initial sample size was estimated using the sample size formula for prevalence studies [46] given by $n = N*X / (X + N - 1)$, where $X = Z^2*p*(1-p) / MOE^2$, and $Z=Z\alpha/2$ is the critical value of the normal distribution at $\alpha/2$ (for confidence level of 95%, α is 0.05 and critical value is 1.96), MOE is the margin of error (5%), p is an estimate of UGS prevalence in the study area (fixed at 55%), and N is the population of females in the study area (1400). The Finite Population Correction was applied to the sample size formula. Thus, $n = 1400*3.8 / (3.8 + 1400-1) = 387$. With an originally determined sample size of 387, due to logistic and cultural constraints, 304 (78.55%) of target recruitment was reached [33].

A secondary objective in this study was also to find out reproductive health determinants for FGS. For that, a sub-sample of 67 females was obtained from the 304 women enrolled in the study (Figure 1). Eligibility criteria for this sub-group consisted of the following: being 14 years old (considered as minimum marriage age in this context) and above, not virgin, not menstruating at present, not pregnant, and consent/assent from parent or spouse for girls younger than 18. Hence, of the 304 participants enrolled and tested for UGS, 193 were eligible for clinical FGS assessment based on age (Figure 1). However, due to participant availability, logistic constraints, and consent amongst others, only 67 amongst 193 participants were available for clinical FGS diagnosis.

Questionnaires related to sexual and reproductive health characteristics were administered to participants based on age and question sensitivity. Hence, varying denominators for different variables.

Due to the secluded nature of study communities (far from health care settings), and the preference of a participative nature for recruiting (involvement of formal/informal health workers and some community members), recruitment was contextualized within each community as per the propositions of key community members (including participants themselves).

Within the sub-group for FGS diagnosis, after questioning (questionnaire), consenting participants underwent gynecological examination by colposcopy with photo documentation by a trained midwife. All participants were recruited and screened within the community, mostly in their homes or a 'safe' house prescribed by the women themselves, or the village leader.

Figure 1: Study participant selection criteria and numbers with diagnostic methods flow

Thus, after UGS assessment, a structured questionnaire (see Supplementary File 1) with FGS related symptoms [33], sexual and reproductive health, and socio-demographic questions, was administered privately in a one-to-one format to all consenting/assenting participants, mostly based on age and question sensitivity. For girls younger than 14, questions linked to sexual health were avoided, and other questioning also depended on parent/guardian availability for aiding/complementing their responses or responding directly for them. For girls/women older than 14, both reproductive and sexual health related questions were asked where possible. Participants responded to the structured questionnaire and were prompted to discuss further on related symptoms if they wished to share.

Sexual and reproductive health related questions included: sexual activeness, (with age of first encounter or age at marriage), number of children, age of last child, any miscarriage, menstrual irregularities or abnormalities (collected as irregular, painful or ceased menstruation), abdominal pain, coital pain, and vaginal itches with abnormal discharges. Demographic questions asked included: age, level of formal or informal schooling achieved, water contact activities, and income generating activities. Most females encountered during initial sample enrolment were married by age14, which helped guide the minimum age for the study, in terms of deciphering a general baseline for assessing girls for FGS (through general

sexual health related questions, and invasive gynecological examination). Also, age at marriage was used to determine/suggest sub-fertility amongst participants as the age of first child, last child and presence or absence of children was deciphered from the number of years in marriage (or being sexually active) [33, 47]. Hence, sub fertility was considered as marriage age + youngest child= 4+, while infertility referred to marriage age + no child. To better explore age-related profiles, three age groups were formed around these context specific sexual and reproductive health characteristics: adolescence (14-19), young adults (20-35) and older adults (36+).

Parasitological and Gynecological Examinations

Dipstick diagnosis of microscopic hematuria[48], and urine syringe filtration technique with microscopic-based poly-carbonate filter examination for urinary eggs, were used on a single urine sample for standard UGS detection within this study. At least 10 ml of urine was collected and observed for macrohematuria, tested for microhematuria and proteinuria with reagent strips (Siemens Multistix 10 SG), then analyzed for *S. haematobuim* eggs, at the local health center laboratory on the same day of collection. Microscopy for visualization of schistosome eggs was performed by x100 mag. using a light compound microscope and stained with Lugol's iodine. A urine sample was counted positive for UGS on the presence of hematuria[3] or at least one terminal-spined ovum seen[49]. The number of ova reported where classified as ≥50 (high intensity) or < 50 (low intensity)[2]. Next, consenting eligible girls and women were examined by clinical colposcopy with photo-documentation, using a hand-held colposcope (EVA COLPO, Mobile ODT). The obtained images were cross-checked against the WHO FGS pocket atlas[5] to record key sequelae. These were then saved in a coded database for the internal validation through blinded evaluation of cervical images from photo-colposcopy by external team members, following the cross examination with the WHO Pocket atlas. A minimal clinical indication for FGS was determined upon the presence of sandy patches, abnormal blood vessels and/or sandy patches on homogenous yellow areas, in line with the WHO FGS pocket atlas coding[5] after cross verification by external specialists.

Statistical Analysis

All numerical data collected were first imputed into computer system using the Microsoft excel database and later imported into the R (version 4.0.2) software for statistical analyses. In univariate analysis, frequencies and proportions were reported for socio-demographic, syndromic and clinical variables. In bivariate analysis, Pearson's chi-squared tests were used to test the association between the socio-demographic, clinical and syndromic reproductive health related variables (which serve as independent variables), against the dependent variables FGS and UGS. To further highlight such dependence, univariate logistic regression analyses was used, with the results presented in the form of unadjusted odds ratios. To identify most relevant variables amongst the reproductive health related independent variables associated to each of UGS and FGS, multivariate logistic regressions analyses were used, with the results presented in the form of adjusted odds ratios (AOR), alongside 95% confidence intervals (CI) and *p*-values based on the Wald's Test. To fit the models, only factors significantly related to the outcomes at a 25% level of significance in the univariate models were included. Multicollinearity between independent variables in the initial multivariate models were evaluated using the `vif` function in the `car R` package and our knowledge on how the variables were measured. The step function in the `R` package `stats` was applied to the resulting multivariate models after correcting for multicollinearity to select the "best" fitting model. The global significance of variables in the final models were evaluated based on analysis of deviance tables using the `anova` function in the `stats R` package. In all, the level of significance was set at *p*-value <0.05.

Results

A. General participant characteristics

A total sample population of 304 females were enrolled, and all diagnosed for UGS, aged from 5 to 69 years old (193 of reproductive age, >13 and <70, with mean±SD age of 28 ±12.7). Also, 88.16% of participants were dependent on, and lived within a proximity of ≤200m to the Mape lake (Island

communities), and the remaining 11.82% came from Mainland communities, which were further from the lake (>400m), having alternative water sources (wells and stand taps), and involved in farming alone without fishing activities. A prevalence of 63.8% (194/304) for UGS was recorded from egg prevalence or hematuria. Furthermore, 27.30% showed proteinuria, and a 51.0% prevalence (155/304) was recorded for hematuria (with 19 showing macrohematuria). Microhematuria sensitivity and specificity was calculated against egg positivity, with a specificity and sensitivity of 80.00% (95% CI: 73.58 – 86.42) and 73.83% (95% CI: 66.91 – 80.75) respectively. The Geometric Mean Egg (GME) count was 33.1 (Range: 2 – 1220) among which 36.2% had heavy (≥ 50 eggs/10ml of urine) infection while 63.8% had light (> 50 eggs/10ml of urine) infection. Macrohematuria was strongly related to egg density categories ($\chi 2 = 17.7$; $P < 0.001$), where cases of macrohematuria were directly related to heavy egg load (93.2%). Information related to sub fertility/infertility was captured based on age at marriage, number of children and the age of last child; with more than half of the study population reporting not having received treatment with praziquantel in more than a year (see Table 1). Reported sexual and reproductive health syndromes included miscarriages (58.89%), lower abdominal pain (56.95%), lower back pain (44.59%), coital pain (45.98%), coital bleeding (37.93), vaginal itches (68%), abnormal vaginal discharge (42.6%) and menstrual irregularities (47.74%), all seen to be comparatively higher amongst participants, compared to stress incontinence (19.47) (see Table 1).

Table 1: General characteristics of all study participants (Sociodemographic, syndromic, clinical)

Variable	Category	Number of Women	Percentage
1. Demographic			
Age (groups) *(n=304/304*)*	<14	111	36.51
	[14-20[	62	20.39
	[20-36[	83	27.3
	36+	48	15.79
Menarche*(n=304/304*)*	Pre	98	32.24
	Post	206	67.76
Age at marriage *(n=178/193*)*	[13-15[	71	39.89
	[15-18[	88	49.44
	18+	19	10.67
No of Children *(n=181/193*)*	0	44	24.31
	[1-3]	72	39.78
	[26]	37	20.44
	7+	28	15.47
Age of last child *(n=130/137*)*	0+	10	7.69
	[1-3]	67	51.54
	[26]	15	11.54
	7+	38	29.23
Treatment with praziquantel *(n=304/304*)*	< 12 months	1	0.3
	> 12 months	292	96.1

	Never	11	3.6
Economic Activity *(n=241/304*)*	Fishing (with/without farming)	211	87.5
	Farming (without fishing)	30	12.4
Proximity to lake *(n=304/304*)*	<200m	268	88.16
	>400m	36	11.84
2. Syndromic			
Lower Abdominal Pain*(n=223/304*)*	Yes	127	56.95
Coital Pain*(n=174/193*)*	Yes	80	45.98
Coital bleeding*(n=174/193*)*	Yes	66	37.93
Vaginal Itches*(n=225/304*)*	Yes	153	68.00
Vaginal Discharge*(n=214/304*)*	Yes	90	42.06
External genital Itch*(n=206/304*)*	Yes	86	41.75
Lower back Pain*(n=223/304*)*	Yes	99	44.59
Stress Incontinence*(n=226/304*)*	Yes	44	19.47
Menstrual Irregularities*(n=199/206*)*	Yes	95	47.74
Fertility*(n=178/193*)*	Sub fertility	158	88.8%
	Infertility	20	11.2%
Miscarriages*(n=180/193*)*	0	74	41.11
	1+	106	58.89
3. Clinical			
Parasitemia*(n=304/304*)*	0	141	46.38
	[1-50]	104	34.21
	50+	59	19.41
Hematuria*(n=304/304*)*	+	155	51.0
Proteinuria*(n=304/304*)*	+	83	27.30

*Shows the eligible sample size for each variable. For age of marriage (*n=178/193**) for example, 178 out of the 193 eligible women gave information their marriage age, meaning 15 women had missing information for the variable.

1. UGS Characteristics amongst sample population

Table 2 presents the relationship between UGS as a dependent factor and each of the sociodemographic and reported reproductive health characteristics based on chi-square tests of independence and univariate logistic regression. The results indicate that the chances of UGS infection amongst women who lived more than 400m from the lake was 0.36 (95% CI: 0.17-0.72) times that of women who lived less than 200m to the lake, implying that significant odds of being infected with UGS was seen with closer lake proximity. A significant decrease in chances of infection with urogenital schistosomiasis was observed with increasing age. Relative to girls <14 years, girls between 14-19 years had a 0.46 (95% CI: 0.22-0.95) odds of having UGS, as opposed to 0.29 (95% CI: 0.15-0.54) odds for adults ranging from 20-35 years, and 0.09 (95% CI: 0.04-0.19) odds for women older than 35 years. All reported reproductive health syndromes showed significant relationship with UGS, except for stress incontinence (UOR 1.72 [95% CI: 0.87-3.54] p= 0.1287). In effect, women with lower abdominal pain, coital pain, vaginal itch, menstrual irregularity, and coital bleeding showed significantly higher odds (Table 2) of UGS.

Table 2: Relations between UGS and each socio-demographic and syndromic variable in the study sample

Variables	Category	n	Chi2 test of Independence			Univariate logistic regression			
			UGS – n (%)	UGS + n (%)	P-value	Unadjusted OR (95% C.I.)			P value
Age group	<14	111	20 (18.2)	91 (46.9)		1			
	[14-20[	62	20 (18.2)	42 (21.6)		0.46	(0.22,	0.95)	0.0352
(n=304)	[20-36[	83	36 (32.7)	47 (24.2)		0.29	(0.15,	0.54)	0.0002
	36+	48	34 (30.9)	14 (7.2)	<0.0001	0.09	(0.04,	0.19)	<0.0001
No of Children	0	44	15 (18.1)	29 (29.6)		1			
(n=181)	[1-3]	72	33 (39.8)	39 (39.8)		0.61	(0.28,	1.32)	0.2143
	[4-6]	37	16 (19.3)	21 (21.4)		0.68	(0.27,	1.67)	0.3994
	7+	28	19 (22.9)	9 (9.2)	0.0462	0.25	(0.09,	0.66)	0.0063
Age of Last Child	0+	10	4 (6)	6 (9.5)		1			
(n=130)	[1-3]	67	33 (49.3)	34 (54)		0.69	(0.16,	2.62)	0.5863
	[4-6]	15	4 (6)	11 (17.5)		1.83	(0.33,	10.6)	0.4862
	7+	38	26 (38.8)	12 (19)	0.0323	0.31	(0.07,	1.27)	0.1082
Miscarriages	0	74	41 (48.8)	33 (34.4)		1			
(n=180)	1	52	19 (22.6)	33 (34.4)		2.16	(1.05,	4.52)	0.0382
	2+	54	24 (28.6)	30 (31.2)	0.1055	1.55	(0.77,	3.17)	0.2216
Lower Abdominal Pain*(n=223)*	Yes	127	42 (45.2)	85 (65.4)	0.0039	2.29	(1.33,	3.98)	0.0028
Coital Pain*(n=174)*	Yes	80	25 (30.5)	55 (59.8)	0.0001	3.39	(1.82,	6.43)	0.0001
Coital bleeding*(n=174)*	Yes	66	19 (23.2)	47 (51.1)	0.0002	3.46	(1.82,	6.79)	0.0002
Vaginal Itches*(n=225)*	Yes	153	51 (53.7)	102 (78.5)	0.0001	3.14	(1.77,	5.67)	0.0001
Abnormal Vaginal Discharge *(n=214)*	Yes	90	27 (29)	63 (52.1)	0.0008	2.66	(1.51,	4.76)	0.0008
Lower Back Pain*(n=222)*	Yes	99	34 (36.6)	65 (50.4)	0.0551	1.76	(1.03,	3.06)	0.0416
Stress Incontinence*(n=226)*	Yes	44	14 (14.7)	30 (22.9)	0.1729	1.72	(0.87,	3.54)	0.1287
Genital Itches*(n=206)*	Yes	86	26 (28.6)	60 (52.2)	0.0007	2.73	(1.53,	4.94)	0.0008
Menstrual Irregularity*(n=199)*	Yes	95	29 (33)	66 (59.5)	0.0002	2.98	(1.68,	5.4)	0.0002
Proximity to lake	<20m	268	89 (80.9)	179 (92.3)		1			
	>200m	36	21 (19.1)	15 (7.7)	0.0051	0.36	(0.17,	0.72)	0.0042

Multivariate Logistic Regression Model for Reporting Sexual and Reproductive Health (SRH) Risk Factors related to UGS

After including all variables significantly related to UGS at a 25% level in a multivariate model, multicollinearity issues were suspected between lower abdominal pain and lower back pain, and external genital itch and vaginal itches. However, considering genital itch responses were most often related to vaginal itch or misreported by respondents due to their literal similarity in Pidgin English or Fulbe used during questioning, we resorted to keeping only vaginal itches in the model. Similarly for lower back pain and lower abdominal pain because of the similarity in responses, but with a more comprehensive responding for lower abdominal pain, lower back pain was removed. The resulting "best" fitting model included age group, lower abdominal pain, and coital pain as the most significant sexual and reproductive health risk factors for UGS (Table 3). In this result, we also observed a decreasing trend in

number of cases of UGS with increasing age. Also, the odds of infection in women with lower abdominal pain was 6.42 (95% CI: 2.85 - 15.68) times that for women without the pain. The odds of infection in women with coital pain was 2.16 (95% CI: 1.05 – 4.46) times that for women without the pain.

Table 3: Possible risk factors for UGS amongst the socio-demographic and SRH included in the study. A multivariate logistic regression model on the effects of sexual and reproductive health factors significantly related to UGS.

SRH Indicator	Category	Adjusted OR (95% C.I.)	P value
Age group	[14-20[	1.0	
	20-36[	0.28 (0.10, 0.70)	0.0087
	36+	0.11 (0.04, 0.31)	0.0001
Lower Abdominal Pain	No	1.0	
	Yes	6.42 (2.85, 15.68)	0.0000
Coital Pain	No	1.0	
	Yes	2.16 (1.05, 4.46)	0.0362

2. FGS Characteristics amongst study participants (Sub-group)

Of the total number of participants examined for FGS after UGS (n=67), 40 were confirmed to have ova-patent UGS, and 34 for FGS, upon the presence of homogenous yellow sandy patches, grainy sandy patches, and abnormal blood vessels (Figure 2). A breakdown of UGS/FGS within the subset of 67 women examined for FGS showed: 26 FGS+/UGS+; 8 FGS+/UGS-; 14 FGS-/UGS+; and 19 FGS-/UGS-. Related reproductive health syndromes (as reported in UGS), similarly, were all found to have some association ($P < 0.05$) with FGS manifestation amongst females (Table 4), except for stress incontinence. Of import amongst these, menstrual irregularities or abnormality, also found with UGS, was seen to have 7.9 times higher odds of affecting women with FGS than women without FGS (Table 4). Back pain was seen to significantly affect women with FGS manifestations than was the case with UGS. Similarly, odds of having FGS manifestations were seen to ascend with age (Table 4), unlike UGS which was significant with descending age. Lower abdominal pain, menstrual irregularity and lower back pain showed the highest odds of manifesting amongst women with FGS.

Figure 2: Imagery of FGS pathology of the cervix with reported lesions (magnification x4)

A) 1-rubbery papule, 2-abnormal blood vessel, 3- homogeneous sandy patch (30-year-old woman, +UGS, +lower abdominal pain, +Menstrual irregularity); **B**) 1,2- grainy sandy patches (45-year-old woman, -UGS, +lower abdominal pain; +Menstrual irregularity)

Table 4: Relations between FGS and socio-demographic and syndromic variables in the sub-group of girls and women diagnosed for FGS

Variables*(n=67)*	Category	N	Chi2 Test of Independence			Univariate logistic regression			
			FGS – n(%)	FGS + n(%)	P-value	Unadjusted OR (95% C.I.)			P value
Age group	[14-20[	19	15 (45.5)	4 (11.8)		1			
	[20-36[	29	11 (33.3)	18 (52.9)		6.14	(1.73,	26.1)	0.0077
	36+	19	7 (21.2)	12 (35.3)	0.0091	6.43	(1.62,	30.35)	0.0116
Age at Marriage	[13-15[	23	10 (30.3)	13 (38.2)		1			
	[15-18[	38	22 (66.7)	16 (47.1)		0.56	(0.19,	1.58)	0.2765
	18+	6	1 (3)	5 (14.7)	0.1286	3.85	(0.51,	79.99)	0.2510
No of Children	0	16	12 (36.4)	4 (11.8)		1			
	[1-3]	22	12 (36.4)	10 (29.4)		2.5	(0.64,	11.23)	0.2024
	[4-6]	15	4 (12.1)	11 (32.4)		8.25	(1.79,	46.95)	0.0102
	7+	14	5 (15.2)	9 (26.5)	0.0363	5.4	(1.19,	28.98)	0.0357
Age of Last Child	0+	1	1 (4.8)	0 (0)		1			
	[1-3]	27	14 (66.7)	13 (46.4)		Inf	(0,	Inf)	0.9965
	[4-6]	4	0 (0)	4 (14.3)		Inf	(0,	Inf)	0.9937
	7+	17	6 (28.6)	11 (39.3)	0.1199	Inf	(0,	Inf)	0.9963
Miscarriages	0	26	18 (54.5)	8 (23.5)		1			
	1	22	8 (24.2)	14 (41.2)		3.94	(1.22,	13.78)	0.0256
	2+	19	7 (21.2)	12 (35.3)	0.0362	3.86	(1.14,	14.19)	0.0343
Lower Abdominal Pain	Yes	47	15 (45.5)	32 (94.1)	0	19.2	(4.74,	131.08)	0.0003
Coital Pain	Yes	32	10 (30.3)	22 (64.7)	0.0071	4.22	(1.55,	12.16)	0.0058
Coital bleeding	Yes	29	8 (24.2)	21 (61.8)	0.0029	5.05	(1.82,	15.19)	0.0026
Vaginal Itches	Yes	49	18 (54.5)	31 (91.2)	0.0009	8.61	(2.44,	40.95)	0.0021
Vaginal Discharge	Yes	32	9 (27.3)	23 (67.6)	0.0014	5.58	(2.01,	16.67)	0.0013
Back Pain	Yes	41	12 (36.4)	29 (85.3)	0	10.15	(3.31,	36.45)	0.0001
Stress Incontinence	Yes	10	0 (0)	10 (29.4)	0.0009	Inf	(0,	Inf)	0.9927
Genital Itch	Yes	32	9 (27.3)	23 (67.6)	0.0014	5.58	(2.01,	16.67)	0.0013
Menstrual irregularities	Yes	34	9 (27.3)	25 (73.5)	0.0002	7.41	(2.61,	23)	0.0003
Proximity	<20m	60	30 (90.9)	30 (88.2)	1	1			
	>200m	7	3 (9.1)	4 (11.8)	1	1.33	(0.27,	7.25)	0.7212

Multivariate Logistic Regression Model for Reporting Sexual and Reproductive Health (SRH) Risk Factors related to FGS

Similar to UGS, a multivariate model was constructed with all variables significantly related to FGS at a 25% level. As well, multicollinearity checks revealed lower back pain and genital itch (for same reasons) with the variables age group, coital pain, vaginal itches, and lower abdominal pain (Table 5) retained in the "best" fitting model.

Table 5: Possible risk factors amongst SRH for FGS. A multivariate logistic regression model on the effects of FGS on sexual and reproductive health factors.

SRH Indicator	Category	Adjusted OR (95% C.I.)	P value
Age group	[14-20[		
	[20-36[	20.15 (2.92, 240.94)	0.0061
	36+	41.29 (4.16, 946.69)	0.0054
Coital Pain	No	1.0	
	Yes	10.44 (2.12, 90.91)	0.0105
Vaginal Itches	No	1.0	
	Yes	12.50 (1.92, 128.77)	0.0151
Lower Abdominal Pain	No	1.0	
	Yes	28.80 (3.36, 578.24)	0.0081

3. UGS, FGS and associations with reproductive health characteristics

Age, number of children, age of last child, menstrual abnormality, miscarriages, and lower abdominal pain were identified as possible reproductive health factors associated with *S. haematobium* infection and were used within this study. Generally, both FGS and UGS were not significantly (*P*-value >0.05) related to number of children, age of last child and miscarriages. In multivariate logistic regression models, after selection of the best fitting models, the results show that the most significant risk factors for UGS are age group, lower abdominal pain and coital pain (Table 4), whereas age-group and lower abdominal pain, coital pain and vaginal itches were identified as the most significant risk factors for FGS (Table 5).Chances of FGS manifestations amongst women with lower abdominal pain was AOR 9.5(95% CI:1.7-81.8) times that of women without the pain (Table 5). Analysis of deviance tables for both best fitting models (FGS and UGS), with *p*-values based on likelihood ratio tests are reported in Supplementary File 2.

Discussion

Understanding the risks and associations of UGS and FGS, especially within different contexts of women's health[41, 50], sheds greater light on the disease epidemiology, which could foster improved and coordinated control measures both locally and nationally[41]. Furthermore, precisely documenting existing associations between both UGS and FGS could clarify further the need for precision mapping

of schistosomiasis in endemic regions, for formulating a better targeted integrated response[48]. Though a non-significant association was observed between egg intensity in urine and FGS from the onset of this study (Table 2), parasitemia association has been shown to be misleading in UGS[7, 12, 13] from several other studies[13] and reports on FGS, particularly when only a single urine sample is examined which is usually the case for population-based surveillance[6]. Considering this, questionnaire (for symptoms)[10, 21], as well as visual examination of cervix and vaginal walls by colposcopy[12, 18, 51], offers an added strength to single sample urinalysis for detection of FGS, as carried out in this study, and several others[10, 18]. The possibility of the presence of FGS in UGS populations has been often raised[8, 21],with projections of about 360 million girls and women possibly having UGS[15], but today it is thought that at least 56 million adolescent girls and women are suffering from FGS[15, 17]. Our results seem to show an even higher rate of FGS amongst the UGS infected population with an approximate FGS/UGS ratio of 34/40. Our study, given our application of portable colposcopy, is the first formal attempt to document the pathology of FGS in a primary care setting in Cameroon.

Elsewhere, the clinical pathology of FGS has been described resulting from the complex inflammatory responses to antigens released by adult worms and viable eggs[6, 14], which persists until sometime after adult worms are stopped egg-laying or are destroyed by praziquantel[24]. Thereafter, various signs and symptoms (or effects) may present months or even years after treatment[23, 42].

From present results, and within the general literature[15, 17], one of such effects noted is an effect on menstrual health. More than half of women within the study who reported poor menstrual health (FGS = 73.5%; UGS = 54.6%), either as irregular, painful or seized menstruation, were found to either shed eggs in urine (positive for UGS), or were positive for FGS, but without eggs in urine; showing more women positive for FGS reporting abnormal menstruation, than for UGS. This confirms recent analysis[17, 33] and suggests strong linkages between menstrual health management and FGS[15, 17], an under researched area. This can be credited to the fact that symptoms perhaps diminished after a while with UGS (maybe as a result of treatment in mass drug administration campaigns), but later resurface with more chronic sequelae of FGS[17], and with more dire symptoms and negative impact on menstrual health[17, 33]. In our study context, post-menarche females already faced a substantial

challenge with limited access to hygienic material and information on menstrual health management, typically relying on self-made clothes and absorbent plant leaves during menstruation, due to lack of finances or general knowledge.

Still related to FGS and menstrual health, narratives from a previous study[33] which used qualitative probing showed women having manifestations of FGS and not shedding eggs in urine, gave a history of having lived in their earlier years in heavily infested *S. haematobium* foci. This explained their later manifestation of FGS symptoms, even after having moved away to a less infested area, with more than 90% limit in fresh water contact[33]. This is similar to our findings, where lake proximity was seen to be not very significant to FGS manifestation (Table 4), same as egg shedding, still pointing to early-in-life infection and later chronicity. Significant difference in menstrual abnormalities amongst UGS positive women [n=22(56.4)] and UGS negative women [n=12 (44.4)], alerts to future chronicity of FGS after UGS, especially if not managed with more readily available praziquantel treatment(s)[42, 52].

On its own, lower abdominal pain observed significant association (in adjusted and unadjusted regression models) in both UGS and FGS. The chances of having lower abdominal pain were significantly higher in females with either FGS (94.1%) or UGS (84.2%). Similarly with coital pain and vaginal itches, these reported as key indicators for UGS and FGS, directing early diagnosis of UGS and future FGS in endemic communities, thereby promoting the verticalization of control strategies for both diseases.

Another trend observed in this study is that intensity of infection or egg patent-prevalence (for UGS) reduces while chronic disease or morbidity for FGS increases as women age. The chances of FGS after UGS increased significantly (AOR 6.43,95% C.I 1.62-30.35, P=0.0091) as women aged (36+). Similar findings have been reported in other studies in different geographical locations[6, 14, 53, 54] and recently in this area[33]; emphasizing on the level of present intensity for UGS, and possible future occurrence of FGS[14, 54]. UGS at a younger age will in some cases manifest into FGS when the female is older[14], causing more intense gynecological symptoms and effects. This offers a possible guiding tool for better control policies, related to early diagnosis and treatment[41, 55]. This surpasses need

alone for school-based MDAs[13, 28, 56], but considers and encourages individual therapy in different contexts for FGS (and MGS)[6].

Although only a few amongst the extensive list of reproductive health determinants [54] were identified in this study to be statistically significant, where mostly reported symptoms were collected, clinical and biological examinations carried out, enabled confirmation of how future self-reported symptoms with UGS and FGS might be best used[33]. These results support the advocated need for further attention on post-transmission schistosomiasis[57], and also, the availability of praziquantel in lowest level (Health Areas and community) health care for individual therapy[54], as well as treatment from a younger age[15, 28, 41, 52], buoyed with the recent development of pediatric praziquantel[58].

Study Limitations

Though described as gold standard[49], active UGS was only detected through observation of eggs in urine samples by microscopic-based poly-carbonate filter examination, as well as recommended dipstick assays for urinary hematuria detection. Alternative molecular assays such as polymerase chain reaction (PCR) for schistosome detection in human serum and urine samples[12], were not considered for added sensitivity for UGS and FGS (in vaginal lavage analysis)[3, 59]. Though recommended[12, 21], only visual examination through inspection for lesions on the cervix, the fornices, and the vaginal walls with a colposcope[5, 51] and screening with questionnaires[10] was considered in the detection of FGS in this study. Lastly, clinical diagnosis of FGS was carried out only on a limited sub-group of females, where more precise conclusions may be obtained by using an appropriate sample size.

Conclusion

Whilst millions of women in Cameroon have UGS, its epidemiological connection with FGS is not fully appreciated, which creates an unfortunate knowledge holdup for effective control at the public health level. In our chosen study location, which is broadly typical for endemic areas of UGS in Cameroon[21, 34, 36, 40], strong epidemiological associations between UGS and FGS were found against certain key sexual and reproductive determinants: age, lower abdominal pain and menstrual health. This formative knowledge could be utilized to tackle and ultimately prevent FGS, with a more

targeted integrated control for UGS in Cameroon and elsewhere in endemics areas for UGS globally. This study further adds detailed insight into the connection of FGS and UGS within primary care in endemic communities, denoting those with cardinal symptomologies more explicitly for scalable detection and targeted control of FGS within UGS endemic areas.

Supporting Files

Supplementary File 1.docx : Structured questionnaire

Supplementary File 2.docx: Deviance Table

Declarations

- **Authors' contributions**

MCM and JRS conceptualized the study and planned the methodology; AEN,VG, MCM, carried out field investigation; MCM, FNB, JRS, ASO, AEN, analyzed and interpreted the data for this manuscript; MCM acquired funding for study and wrote the original draft of the manuscript; JRS supervised the study and was a major contributor in the conceptualization and writing of the manuscript; AEN, coordinated field activities within the Malanteoun Health District; AEN, FNB, VG, ASO, reviewed and edited the manuscript. All authors approved the final version of the paper before submission**.**

- **Competing interests**

The authors declare that they have no competing interests.

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- **Data Sharing Statement**

All data generated or analysed during this study are included in this published article [and its supplementary files].

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- **License Statement**

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- **Consent for publication**

Written informed consent for publication of clinical details and/or clinical images was obtained from the patients and parents/guardians where needed.

References

1. Freer JB, Bourke CD, Durhuus GH, Kjetland EF, Prendergast AJ. Schistosomiasis in the first 1000 days. The Lancet Infectious Diseases. 2018;18(6):e193-e203.
2. WHO. Prevention and Control of Schistosomiasis and Soil Transmitted Helminths Geneva: WHO; 2002 [33/63]. Available from: http://apps.who.int/iris/bitstream/handle/10665/42588/WHO_TRS_912.pdf;jsessionid=297C20DDFCBFFF9F9AAE9DF120C0F834?sequence=1.
3. Utzinger J, Becker SL, van Lieshout L, van Dam GJ, Knopp S. New diagnostic tools in schistosomiasis. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2015;21(6):529-42.
4. Søfteland S, Sebitloane MH, Taylor M, Roald BB, Holmen S, Galappaththi-Arachchige HN, et al. A systematic review of handheld tools in lieu of colposcopy for cervical neoplasia and female genital schistosomiasis. International Journal of Gynecology & Obstetrics. 2021;153(2):190-9.
5. WHO. Female Genital Schistosomiasis: A Pocket Atlas for Clinical Health-Care Professionals Geneva: WHO Press; 2015 [Available from: https://www.who.int/publications/i/item/9789241509299.
6. Kjetland E, Leutscher P, Ndhlovu P. A review of female genital schistosomiasis. Trends in Parasitology. 2012;28(2):58-65.
7. Poggensee G, Kiwelu I, Saria M, Richter J, Krantz I, Feldmeier H. Schistosomiasis of the lower reproductive tract without egg excretion in urine. The American journal of tropical medicine and hygiene. 1998;59(5):782-3.
8. Christinet V, Lazdins-Helds J, Stothard J, Reinhard-Rupp J. Female genital schistosomiasis (FGS): from case reports to a call for concerted action against this neglected gynaecological disease. International Journal for Parasitology. 2016;46(7):395-404.
9. Shams M, Khazaei S, Ghasemi E, Nazari N, Javanmardi E, Majidiani H, et al. Prevalence of urinary schistosomiasis in women: a systematic review and meta-analysis of recently published literature (2016–2020). Tropical Medicine and Health. 2022;50(1):12.
10. Ekpo U, Odeyemi O, Sam-Wobo S, Onunkwor O, Mogaji H, Oluwole A, et al. Female genital schistosomiasis (FGS) in Ogun State, Nigeria: a pilot survey on genital symptoms and clinical findings. Parasitology Open. 2017;3:e10.
11. Hotez PJ, Engels D, Gyapong M, Ducker C, Malecela MN. Female Genital Schistosomiasis. New England Journal of Medicine. 2019;381(26):2493-5.

12. Galappaththi-Arachchige HN, Holmen S, Koukounari A, Kleppa E, Pillay P, Sebitloane M, et al. Evaluating diagnostic indicators of urogenital Schistosoma haematobium infection in young women: A cross sectional study in rural South Africa. PloS one. 2018;13(2):e0191459.
13. Wiegand RE, Fleming FM, de Vlas SJ, Odiere MR, Kinung'hi S, King CH, et al. Defining elimination as a public health problem for schistosomiasis control programmes: beyond prevalence of heavy-intensity infections. The Lancet Global Health. 2022;10(9):e1355-e9.
14. Hegertun I, Gundersen S, Kleppa E, Zulu S, Gundersen S, Taylor M, et al. S. haematobium as a common cause of genital morbidity in girls: a cross-sectional study of children in South Africa. PLoS neglected tropical diseases. 2013;7(3):e2104.
15. UNAIDS. 'No more neglect:Female genital schistosomiasis and HIV. www.unaids.org/en/resources/documents/2019/: UNAIDS; 2019.
16. Hotez P. Speaking of Medicine and Health [Internet]. BLOGS P, editor: PLOS BLOGS. 2013. Available from: https://speakingofmedicine.plos.org/2013/05/06/female-genital-schistosomiasis-fgs-sub-saharan-africas-secret-scourge-of-girls-and-women/.
17. Stothard JR, Odiere MR, Phillips-Howard PA. Connecting Female Genital Schistosomiasis and Menstrual Hygiene Initiatives. Trends in Parasitology. 2020;38(5).
18. Bustinduy AL, Randriansolo B, Sturt AS, Kayuni SA, Leustcher PDC, Webster BL, et al. An update on female and male genital schistosomiasis and a call to integrate efforts to escalate diagnosis, treatment and awareness in endemic and non-endemic settings: The time is now. In: Rollinson D, Stothard R, editors. Advances in Parasitology. 115: Academic Press; 2022. p. 1-44.
19. Majangara Karaga R. Concealed urogenital schistosomiasis causing chronic pelvic pain: A case report. Clinical Case Reports. 2021;9(4):1860-4.
20. Stothard J. Female genital schistosomiasis - icebergs of morbidity ahead? Trends in parasitology. 2012;28(5):174-5.
21. Campbell S, Stothard J, O'Halloran F, Sankey D, Durant T, Ombede D, et al. Urogenital schistosomiasis and soil-transmitted helminthiasis (STH) in Cameroon: An epidemiological update at Barombi Mbo and Barombi Kotto crater lakes assessing prospects for intensified control interventions. Infectious diseases of poverty. 2017;6(1):49-.
22. King C. Parasites and poverty: the case of schistosomiasis. Acta tropica. 2010;113(2):95-104.
23. Kjetland EF, Mduluza T, Ndhlovu PD, Gomo E, Gwanzura L, Midzi N, et al. Genital schistosomiasis in women: a clinical 12-month in vivo study following treatment with praziquantel. Trans R Soc Trop Med Hyg. 2006;100(8):740-52.
24. Treatment of Female Genital Schistosomiasis (FGS) With Praziquantel: A Proof-of-Concept Study (NCT04115072) [Internet]. NIH: ClinicalTrials.gov archive. 2020 [cited 31/01/2022].
25. Brindley PJ, Hotez PJ. Break Out: urogenital schistosomiasis and Schistosoma haematobium infection in the post-genomic era. PLoS Negl Trop Dis. 2013;7(3):e1961.
26. Secor WE, Colley DG. When Should the Emphasis on Schistosomiasis Control Move to Elimination? Trop Med Infect Dis. 2018;3(3).
27. Kukula VA, MacPherson EE, Tsey IH, Stothard JR, Theobald S, Gyapong M. A major hurdle in the elimination of urogenital schistosomiasis revealed: Identifying key gaps in knowledge and understanding of female genital schistosomiasis within communities and local health workers. PLoS neglected tropical diseases. 2019;13(3):e0007207.
28. Faust CL, Osakunor DNM, Downs JA, Kayuni S, Stothard JR, Lamberton PHL, et al. Schistosomiasis Control: Leave No Age Group Behind. Trends Parasitol. 2020;36(7):582-91.
29. World Health Organisation. WHO guideline on control and elimination of human schistosomiasis. https://www.who.int/publications/i/item/9789240041608: WHO; 2022. p. 142.
30. Bergquist R, Yang G-J, Knopp S, Utzinger J, Tanner M. Surveillance and response: Tools and approaches for the elimination stage of neglected tropical diseases. Acta Tropica. 2015;141:229-34.
31. SCI Foundation. FAST PACKAGE PROJECT 2021 [Available from: https://schistosomiasiscontrolinitiative.org/projects/fast-research-project
32. Ndassi VD, Anchang-Kimbi JK, Sumbele IUN, Ngufor LA, Nadege K, Kimbi HK. The epidemiological status of urogenital schistosomiasis among reproductive aged individuals in the Tiko

Health Area- a semi-urban setting in the Mount Cameroon area. PLOS Neglected Tropical Diseases. 2021;15(1):e0008978.
33. Masong MC, Wepnje GB, Marlene NT, Gamba V, Mengue M-T, Kouokam E, et al. Female Genital Schistosomiasis (FGS) in Cameroon: A formative epidemiological and socioeconomic investigation in eleven rural fishing communities. PLOS Global Public Health. 2021;1(10):e0000007.
34. TchuentÉ LAT, N'Goran EK. Schistosomiasis and soil-transmitted helminthiasis control in Cameroon and Côte d'Ivoire: implementing control on a limited budget. Parasitology. 2009;136(13):1739-45.
35. National Program for the control of Schistosomiaisis and intestinal helminthiases MoPHC. Towards elimination of Schistosomiasis and Soil-transmitted Helminthiasis and in Cameroon: A road map for paradigm shift 2021-2030. MINSANTE, Yaoundé: MINSANTE; 2022.
36. National Program for the control of Schistosomiaisis and intestinal helminthiases. Progress Report Cameroon 2013-2019. Yaoundé: MINSANTE; 2019.
37. World Health Organization. Global update on implementation of preventive chemotherapy against neglected tropical diseases in 2018. Weekly Epidemiological Record 2019;94(38):425-38.
38. Crompton DWT, World Health Organization. Preventive chemotherapy in human helminthiasis : coordinated use of anthelminthic drugs in control interventions : a manual for health professionals and programme managers. Geneva: World Health Organization; 2006.
39. Makia C, Ozano K, Tagne M, Tchoffo M, Ngang S, Thomson R, et al. Achieving equity in UHC interventions: who is left behind by neglected tropical disease programmes in Cameroon? Glob Health Action. 2021;14(1):1886457-.
40. Njunda A, Ndzi E, Assob J, Kamga H, Kwenti E. Prevalence and factors associated with urogenital schistosomiasis among primary school children in barrage, Magba sub-division of Cameroon. BMC Public Health. 2017;17(1):618.
41. Deworming adolescent girls and women of reproductive age. Policy Brief [press release]. Geneva: WHO2022.
42. Nour NM. Schistosomiasis: health effects on women. Rev Obstet Gynecol. 2010;3(1):28-32.
43. MINSANTE. Schistosomiasis distribution in Malanteoun Health District NTDmaps.org: MINSANTE; 2018 [Available from: https://ntdmaps.org/.
44. National Institute of Statistics Cameroon. Socio-economic statistics of Cameroon, 2015 Cameroon2004-2014 [Available from: https://cameroon.opendataforafrica.org/SESC2015/socio-economic-statistics-of-cameroon-2015.
45. Keptcheu T, Khan P, Gustave L, Gangue T. Some Haematological Parameters among Urinary Schistosomiasis-Malaria Coinfected Children in Suburb of Malentouen Health District, West Region Cameroon. International Journal of Tropical Disease & Health. 2020:34-44.
46. Daniels W. Biostastistics: A foundation for analysis in the health sciences. New York: Wiley & sons; 1999.
47. Beekhuizen Hv, Sharma S. Subfertility. In: Unkels HvBaR, editor. A Textbook of Gynecology for Less-Resourced Locations. London NW3 3AY, UK: Global Library of Women's Medicine , Sapiens Publishing; 2012. p. 170.
48. Colley DG, Bustinduy AL, Secor WE, King CH. Human schistosomiasis. Lancet (London, England). 2014;383(9936):2253-64.
49. World Health Organisation. Schistosomiasis WHO: WHO; 2022 [cited 2022. Available from: https://www.who.int/news-room/fact-sheets/detail/schistosomiasis.
50. World Health Oganization. Regional Office for the Western Pacific. People Centered Health care: A policy framework. 2007.
51. Kjetland EF, Norseth HM, Taylor M, Lillebø K, Kleppa E, Holmen SD, et al. Classification of the lesions observed in female genital schistosomiasis. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2014;127(3):227-8.
52. Bustinduy AL, Friedman JF, Kjetland EF, Ezeamama AE, Kabatereine NB, Stothard JR, et al. Expanding Praziquantel (PZQ) Access beyond Mass Drug Administration Programs: Paving a Way

Forward for a Pediatric PZQ Formulation for Schistosomiasis. PLOS Neglected Tropical Diseases. 2016;10(9):e0004946.
53. Chetty A, Omondi MA, Butters C, Smith KA, Katawa G, Ritter M, et al. Impact of Helminth Infections on Female Reproductive Health and Associated Diseases. Front Immunol. 2020;11:577516.
54. Stothard JR, Stanton, M, Bustinduy, A, Sousa-Figueiredo, J C, Van Dam, GT, Betson, M, et al.,. Diagnostics for schistosomiasis in Africa and Arabia: A review of present options in control and future needs for elimination. Camnbridge core. 2014(141):1947-61.
55. Richardson ST, Franklin AL, Rome ES, Simms-Cendan JS. Global Health: Urogenital Schistosomiasis in the Adolescent Girl. Journal of Pediatric and Adolescent Gynecology. 2016;29(4):326-32.
56. Oluwole AS, Ekpo UF, Nebe OJ, Akpan NM, Jacob SM, Amazigo UV, et al. The new WHO guideline for control and elimination of human schistosomiasis: implications for the Schistosomiasis Elimination Programme in Nigeria. Infectious Diseases of Poverty. 2022;11(1):111.
57. Giboda M, Bergquist R. Schistosomiasis at the Crossroad to Elimination: Review of Eclipsed Research with Emphasis on the Post-Transmission Agenda. 2022;7(4).
58. Pediatric Praziquantel Consortuim. Contract manufacturing agreement signed for production of new pediatric treatment for schistosomiasis 2021 [Available from: http//:https://www.pediatricpraziquantelconsortium.org/.
59. Sturt A, Webb E, Phiri C, Mweene T, Chola N, van Dam G, et al. Genital self-sampling compared with cervicovaginal lavage for the diagnosis of female genital schistosomiasis in Zambian women: The BILHIV study. PLOS Neglected Tropical Diseases. 2020;14(7):e0008337.

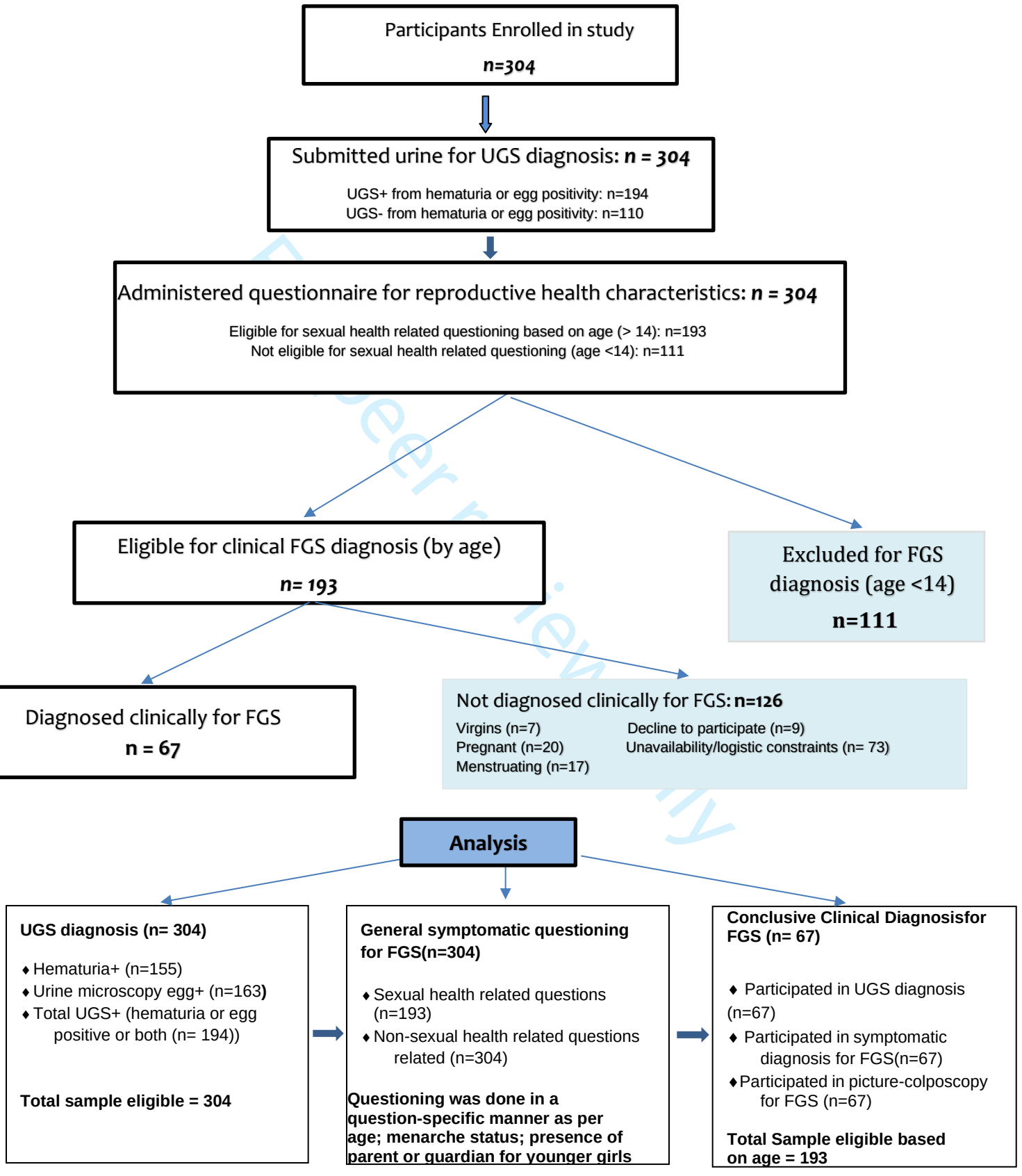
- **Figure Legends**

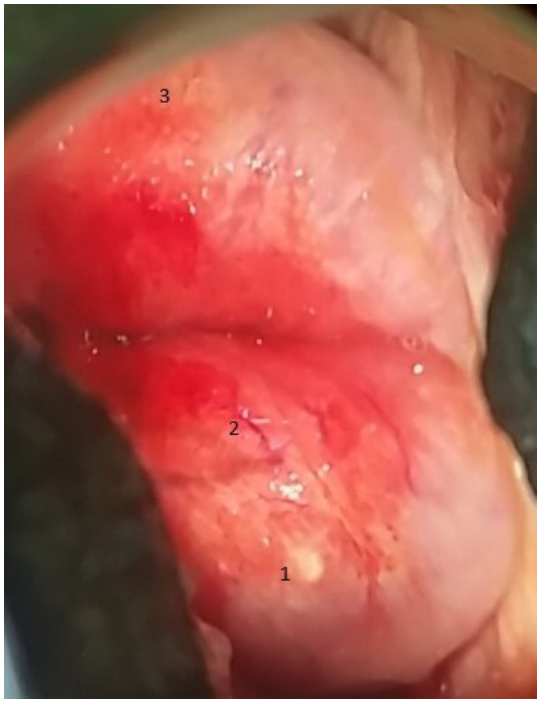
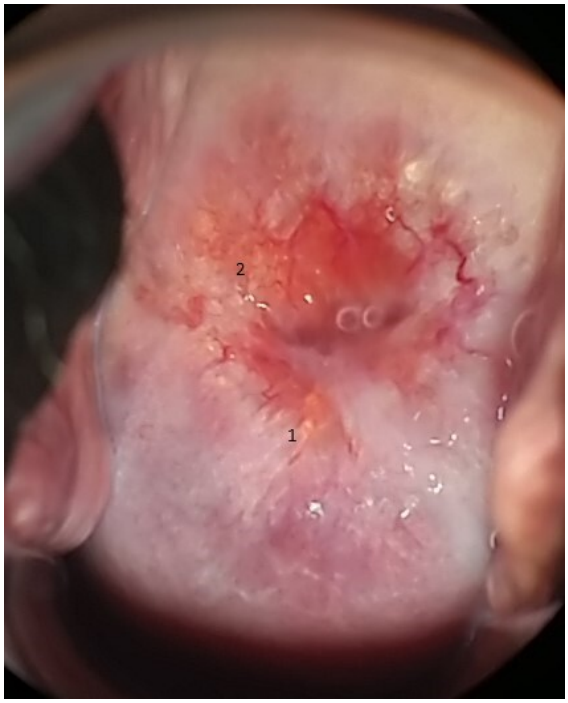
Figure1: Study participant selection criteria and numbers with diagnostic methods flow

Figure 2: Imagery of FGS pathology of the cervix with reported lesions (magnification of x4)

A) 1-rubbery papule, 2-abnormal blood vessel, 3- homogeneous sandy patch (30-year-old woman, +UGS, +lower abdominal pain, +Menstrual irregularity); **B**) 1,2- grainy sandy patches (45-year-old woman, -UGS, +lower abdominal pain; +Menstrual irregularity)

Sampling Flow Diagram



A	B
	

Supplemantary File 1

Close-ended structured questionnaire

A. Close ended structured questionnaire– Administered directly in English with oral translations into Fulbe, Kotoko, Mosgum, and Arab

Name of Community: _____

Age (years): _____

Education: Informal education () Formal education () (specify)_____

Marital Status: Single ( ) Married ( ) Separated ( ) Widowed ( )

No of years having lived in community _____

Previous community _____

Economic activity----------

Residence ---------- (collect coordinates)

Questions on symptoms of urinary tract schistosomiasis; FGS; OR STI

1. Do you see your menses? Yes ( ) No ( )
2. Did you observe/experience your menses within the last two weeks? Yes ( ) No ( ) Does your menses come every month? Regular?
3. Is your menses painful? _____(pain during menstruation – always very painful, sometimes painful, normal) Irregular? _____(every month?, not every month, stopped)
4. Do you have pain in your lower abdomen? When? For how long?
5. Do you have pain when urinating? Yes ( ) No ( )
6. Do you have difficulty in urinating (urine not coming out fluently)? Yes ( ) No ( )
7. Do you have sudden uncontrollable and unexpected urge to urinate and mostly cannot hold it? Even when you cough it comes out? Yes ( ) No ( )
8. Do you see blood in your urine? Yes () No ()
9. (If yes) When did you lastly see blood in your urine? _____Always, sometimes, Once in a while
10. Do you sometimes haveitching in your private part?Yes ( ) No ( )
11. How often do you experience this? Once a while ( ) frequently ( )/ When was the last time?
12. Do you have a feeling of burning within your private part? Yes ( ) No ( )

13. How often do you experience this? Once a while ( ) Frequently ( )

14. Do you sense a swelling/lumps within your private part? Yes ( ) No ( ) No response ( )

15. Do you have any discharge that comes from your vagina? Yes () No () Does it have an ordure? _____ Do you see the colour? Yes ( ) No ( ) What Color is it?White; grey; green/yellow; brown

16. Do you think this is normal? Yes () No() Do not know(). When did you start observing the discharge? Date _____

17. After sexual intercourse do you have a discharge? Yes () No () Is it smelly? Yes () No () Do not know ()

18. After or during sexual intercourse do you have pain?Yes ( ) No ( ) I do not know ( ) ; Do you have a bloody discharge?Yes ( ) No ( ) I do not know ( )

19. Have you had any miscarriages /pregnancies that passed? Yes ( ) No ( )

20. How many? ()

21. Do you have children? Yes() No()

22. What age is your last child? ()

23. Have you visited the clinic to complain about these issues? Yes ( ) No ( )

24. What you used/taken/done to treat any of these problems? _____ (Underline) Hospital or drug store/ local midwife/ traditional medicine/ prayers/ none of the above (what other? Specify)/nothing

Water contact History

1. Where do you fetch your household water? Lake; other source (name) _____
2. Do you fish in the lake? Yes (), No ()
3. Do you bathe in the lake? Yes (), No ()
4. What do you use the lake for? ()_____

Supplementary file 2

Analysis of deviance tables for both best fitting models (FGS and UGS), with *p*-values based on likelihood ratio tests

Variable	Df	Deviance	Resid. Df	Resid. Dev	Pr(>Chi)
UGS					
Age2	2	19.0094	162	208.70	7.450e-05 ***
Lower Abdominal Pain	1	25.6949	161	183.01	3.999e-07 ***
Coital Pain	1	4.4254	160	178.58	0.03541 *
FGS					
Age2	2	9.8057	64	83.061	0.0074253 **
Coital Pain	1	11.3146	63	71.747	0.0007690 ***
Vaginal Itches	1	13.1740	62	58.573	0.0002839 ***
Lower Abdominal Pain	1	10.5961	61	47.976	0.0011333 **

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-6
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	7-10
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	8-9
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	/
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*8-11*
Bias	9	Describe any efforts to address potential sources of bias	/
Study size	10	Explain how the study size was arrived at	7-9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9-10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	7-8
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	/

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	/
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11-13
		(b) Give reasons for non-participation at each stage	7-8
		(c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11-13
		(b) Indicate number of participants with missing data for each variable of interest	/
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	/
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	/
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	/
		Cross-sectional study—Report numbers of outcome events or summary measures	11-13
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9, 12-15
		(*b*) Report category boundaries when continuous variables were categorized	9, 12-15
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	/
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	/
Discussion			
Key results	18	Summarise key results with reference to study objectives	18-20
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	21
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Urogenital Schistosomiasis (UGS) and Female Genital Schistosomiasis (FGS) in Cameroon: An observational assessment of key reproductive health determinants of girls and women in the Matta Health Area

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Title: Urogenital Schistosomiasis (UGS) and Female Genital Schistosomiasis (FGS) in Cameroon: An observational assessment of key reproductive health determinants of girls and women in the Matta Health Area

Authors: Makia Christine Masong[1*], Fesuh Nono Betrand[2], Amabo Elvis Ngwa[3], Victoria A. Gamba[4], Akinola Stephen Oluwole[5], J. Russell Stothard[6]

[1]Department of Social Sciences and Management, Catholic University of Central Africa, Yaoundé, Cameroon

[2]Department of Mathematics and Physical Sciences, National Advanced School of Engineering, University of Yaoundé 1, Cameroon

[3]Malantouen Health District, Malantouen, Cameroon

[4]Department of Obstetrics and Gynecology, University of Nairobi, Nairobi, Kenya

[5]Department of Pure and Applied Zoology, Federal University of Agriculture, Abeokuta, Nigeria

[6]Department of Tropical Disease Biology, Liverpool School of Tropical Medicine, Liverpool, L3 5QA, UK

*Corresponding author

Makia Christine Masong

Department of Social Sciences and Management, Catholic University of Central Africa, Yaoundé, Cameroon

Projet MTN/OCEAC

masongbye@yahoo.com

Abstract

Objectives and Setting: Across sub-Saharan Africa, urogenital schistosomiasis (UGS), in particular female genital schistosomiasis (FGS) is a significant waterborne parasitic disease, with its direct burden upon the sexual and reproductive health (SRH) of sufferers infrequently measured. UGS has an established control plan, which in most endemic regions as in Cameroon, still excludes FGS considerations. Highlighting existent associations between UGS and FGS could increase the management of FGS within UGS interventions. This study seeks to identify current associations amongst FGS and UGS with some reproductive health indicators, to provide formative information for better integrated control.

Participants: 304 females aged 5 - 69 years, were all examined for UGS by urine filtration and microscopy. Amongst these, 193 women and girls were eligible for clinical FGS assessment based on age (>13). After selective questioning for FGS symptoms, a sub-group of 67 women and girls consented for clinical examination for FGS using portable colposcopy, with observed sequelae classified according to the WHO FGS pocket atlas.

Outcome: Overall UGS and FGS prevalence was measured, with FGS/UGS related reproductive health symptoms recorded. Associations between FGS and UGS were investigated by univariate and multivariate logistic regression analyses.

Results: Overall UGS prevalence was 63.8% (194/304), where FGS prevalence (sub-group) was 50.7% (34/67). FGS manifestation increased significantly with increasing age, whilst a significant decrease with ascending age was observed for UGS. Lower abdominal pain (LAP) vaginal itches (VI), and coital pain (CP), were identified as the main significant shared symptoms of both FGS and UGS, while LAP with menstrual irregularity (MI) appeared a strong symptomatic indicator for FGS.

Conclusion: LAP, MI, CP and VI are potential SRH indicators that could be exploited in future for targeting of praziquantel provision to FGS sufferers within primary care, complementary with existing Praziquantel distribution for UGS sufferers in *S. haematobium* endemic areas.

Keywords: *Schistosoma haematobium*, SRH, clinical colposcopy, questionnaires, menstrual health, abdominal pain

Strengths and Limitations of this study

Strengths

- This study used clinical colposcopy, which is the recommended diagnostic method for FGS, though not very common within primary health care settings in sub-Saharan Africa.

- Here, questionnaire approach is used to better capture individual experiences of FGS sufferers within endemic areas for UGS.

Limitations

- Clinical diagnosis of girls younger than 14 (about half of the study participants) was not considered, because of the invasive nature of colposcopy examination, especially as non-invasive clinical diagnostic tools are lacking for examination amongst this age group within low resource schistosomiasis endemic communities.

- Clinical diagnosis for FGS was carried out only on a limited sample

- Assessment for STIs amongst participants are not presented here, whereby such results could complement or clarify FGS diagnosis, considering most sexual and reproductive health related symptoms for urogenital schistosomiasis present as sexually transmitted infections, and can be misdiagnosed.

Introduction

In endemic areas, a definitive diagnosis of urogenital schistosomiasis (UGS) is established by demonstration of viable *Schistosoma (S) haematobium* eggs (≥1) in urine or hematuria[1-3], whilst female genital schistosomiasis (FGS) can be diagnosed visually[4] for *S. haematobium* induced cervical lesions and small fibrotic nodules known as "sandy patches"[5], either with the presence or absence of *S. haematobium* eggs in urine[4, 6, 7]. Whilst both FGS and UGS are caused by infection with *Schistosoma haematobium*[1, 4, 8, 9] a waterborne blood fluke, each appear to have some unclear epidemiological associations, largely due to insufficient disease surveillance[6, 7, 10-13]. In sub-Saharan Africa where UGS is endemic and can be highly prevalent (>50%)[14, 15], insufficient or infrequent efforts have been undertaken to document FGS specifically[11, 16-18], partly as the clinical skills to do so are lacking and uninformed within primary care[10]. While active UGS does not readily predict FGS[6], since FGS can occur without the direct presence of schistosome eggs in urine (a cardinal diagnostic for UGS)[18, 19], rather FGS often presents with a more chronic time frame where schistosome eggs are trapped within the cervico-vaginal surfaces[6, 20, 21]. For some, these trapped eggs can accumulate from very early on in life[1], with enduring and typically hidden sequelae[20, 22]. Based on several biological determinants such as age[1], the mucosal damage and fibrotic scarring of the vaginal and cervical surfaces from FGS proceeds with increasing duration of UGS[6]; moreover, FGS-specific sequelae maybe slow to resolve upon standard antiparasitic treatment of UGS[23, 24], i.e., single annual administration of praziquantel at 40mg/g as used in public health campaigns[6, 13, 20].

In many parts of Africa where surveillance of UGS is limited[25, 26] and that for FGS largely absent[15, 27], there is a clear need to better understand the epidemiological associations between UGS and FGS[14]. Particularly so, to support earlier diagnosis of cases of FGS, and individualize praziquantel treatment needs (for individual and context specific case management)[15, 28] to better avert their disease progression[15]; as current interventions against UGS do not specifically target adolescent girls or women[23, 29]. This gap in treatment coverage[28] and surveillance[13, 30] also has considerable bearing on progress towards elimination of schistosomiasis transmission within disease endemic communities[29].

In recent years, FGS focused research and public health education[31] has gained traction in certain countries such as Ghana, Tanzania, Madagascar, Nigeria, and Mozambique[8, 9], although other countries such as Cameroon, currently lag behind[32, 33]. Schistosomiasis exists in several regions of Cameroon[34], affecting over 10 million people in rural and urban areas[35]. The country has a national coordinated control plan for fairly early interventions during child-hood years (from 5 – 14 years old)[36], which take advantage of school based intervention platforms[37, 38], and in certain settings, community based interventions, where their at-risk status (people or communities dependent on schistosomiasis endemic water bodies, for main water source) is high[21, 32, 36, 39, 40]. Even with improved (>70%) helminth control amongst children in the last decade [35], some of the adolescent at-risk populations do not always benefit from praziquantel treatment due to existing policy gaps and program intervention challenges [[15, 41, 42].

To address this treatment deficit, capture missed opportunities, and ensure the consideration and apprehension of ensuing FGS manifestations within such already identified sub-groups (young girls and women); with better knowledge on the precise associations between UGS and FGS; future control policies and intervention campaigns can be revised to better target at-risk populations.

Here, we sought to clarify existing associations between FGS and UGS, highlighting cardinal symptomologies for scalable detection and targeted control of FGS within UGS endemic areas. This supports the need for a future integrated approach for control of schistosomiasis and limits the "gap" concerning FGS surveillance within current primary care.

Materials and Methods

Ethics approval and consent to participate

Ethical clearance for this study was provided by the Cameroon National Ethics committee on Human Health Research (Ref N ° 2020/07/1266/CE/CNERSH/SP), with administrative authorizations from both the Regional Delegation of Public Health for the West region of Cameroon (Ref N° 679/L/MINSANTE/SG/DRSPO/CBF), and the district Health Office of the Malantouen Health District (Ref N° 078/L/MINSANTE/DRSPO/DSMLT). Informed written and oral consent was obtained from

all participants for parasitological and gynecological examinations. For participants <18 years, parents, husbands, or guardian gave informed permission and assent was obtained from the participants. Privacy and confidentiality of medical information were protected during and after the study.

Patient and Public Involvement

We followed inclusive and participative methods to get overall participant and public involvement. Tailored visits for data collection were carried out according to best practices with local engagement of key community members and local health workers.

Study Setting

This study was carried out across a group of girls and women residing in remote communities surrounding the Mape Dam, a known transmission focus for *Schistosoma haematobium*[35, 40] in the Matta Health Area in Cameroon. Most study participants were involved actively in fishing or other household activity that put them in constant contact with the lake water[33]. More than 90% of the population lived less than 200m to infested water source (the Mape Dam), and more than 75% depended fully on the Mape Dam for house-hold water and for an income generating activity (fishing) [13]. The Matta Health Area hosts several remote fishing island communities that surround this man-made water body, and for at least 18 years has witnessed high transmission of *s. haematobium* with prevalence of UGS greater than 50% amongst children[43].

Study Design and Procedures

This cross-sectional study was conducted between December 2020 and June 2021. The total population estimate of the study site was 5,000 [44], where females represented approximately 51.0%. About 54.6% of the population of females were aged 5-69 years. The sample size estimation for this study was based on UGS prevalence (considered as key indicator for the study). With no existing records of UGS prevalence amongst adults within the Matta Health area, a hypothesis of UGS endemicity amongst adults was based on recorded school-age schistosomiasis prevalence (> 41% in the last decade) within the Matta health Area[43, 45]. In this context made up of primarily fishing communities, more than 80% of adults (both male and female) spent long stretches a day in contact with water (for economic -fishing-

or household activity purposes) [37]. Based on this, we assumed UGS prevalence in such communities should be higher amongst women. Hence, we resorted to an estimate of 55% for UGS prevalence in the Matta health area, for our sample size calculation. Considering lake proximity and economic activities, 11 main communities were involved within the Matta Health Area: nine secluded water-locked fishing communities (Islands/fishing camps) with habitations mostly less than 200m from the lake; and two mainland communities (land-locked) with habitation more than 400m from the lake[33].

Following a simple random sampling technique, on the base of attaining a precision rate of 95% with an error margin of 5%, our initial sample size was estimated using the sample size formula for prevalence studies [46] given by $n = N*X / (X + N - 1)$, where $X = Z^2*p*(1-p) / MOE^2$, and $Z=Z\alpha/2$ is the critical value of the normal distribution at $\alpha/2$ (for confidence level of 95%, α is 0.05 and critical value is 1.96), MOE is the margin of error (5%), p is an estimate of UGS prevalence in the study area (fixed at 55%), and N is the population of females in the study area (1400). The Finite Population Correction was applied to the sample size formula. Thus, $n = 1400*3.8 / (3.8 + 1400-1) = 387$. With an originally determined sample size of 387, due to logistic and cultural constraints, 304 (78.55%) of target recruitment was reached [33].

A secondary objective in this study was also to find out reproductive health determinants for FGS. For that, a sub-sample of 67 females was obtained from the 304 women enrolled in the study (Figure 1). Eligibility criteria for this sub-group consisted of the following: being 14 years old (considered as minimum marriage age in this context) and above, not virgin, not menstruating at present, not pregnant, and consent/assent from parent or spouse for girls younger than 18. Hence, of the 304 participants enrolled and tested for UGS, 193 were eligible for clinical FGS assessment based on age (Figure 1). However, due to participant availability, logistic constraints, and consent amongst others, only 67 amongst 193 participants were available for clinical FGS diagnosis.

Questionnaires related to sexual and reproductive health characteristics were administered to participants based on age and question sensitivity. Hence, varying denominators for different variables.

Due to the secluded nature of study communities (far from health care settings), and the preference of a participative nature for recruiting (involvement of formal/informal health workers and some community members), recruitment was contextualized within each community as per the propositions of key community members (including participants themselves).

Within the sub-group for FGS diagnosis, after questioning (questionnaire), consenting participants underwent gynecological examination by colposcopy with photo documentation by a trained midwife. All participants were recruited and screened within the community, mostly in their homes or a 'safe' house prescribed by the women themselves, or the village leader.

Figure 1: Study participant selection criteria and numbers with diagnostic methods flow

Thus, after UGS assessment, a structured questionnaire (see Supplementary File 1) with FGS related symptoms [33], sexual and reproductive health, and socio-demographic questions, was administered privately in a one-to-one format to all consenting/assenting participants, mostly based on age and question sensitivity. For girls younger than 14, questions linked to sexual health were avoided, and other questioning also depended on parent/guardian availability for aiding/complementing their responses or responding directly for them. For girls/women older than 14, both reproductive and sexual health related questions were asked where possible. Participants responded to the structured questionnaire and were prompted to discuss further on related symptoms if they wished to share.

Sexual and reproductive health related questions included: sexual activeness, (with age of first encounter or age at marriage), number of children, age of last child, any miscarriage, menstrual irregularities or abnormalities (collected as irregular, painful or ceased menstruation), abdominal pain, coital pain, and vaginal itches with abnormal discharges. Demographic questions asked included: age, level of formal or informal schooling achieved, water contact activities, and income generating activities. Most females encountered during initial sample enrolment were married by age14, which helped guide the minimum age for the study, in terms of deciphering a general baseline for assessing girls for FGS (through general

sexual health related questions, and invasive gynecological examination). To better explore age-related profiles, three age groups were formed around these context specific sexual and reproductive health characteristics: adolescence (14-19 years), young adults (20-35 years) and older adults (36+ years). The first age group can be considered to represent active marriage period in this study area, the second, period of high conception probability, and third, post conception period [47].

Parasitological and Gynecological Examinations

Dipstick diagnosis of microscopic hematuria[48], and urine syringe filtration technique with microscopic-based poly-carbonate filter examination for urinary eggs, were used on a single urine sample for standard UGS detection within this study. At least 10 ml of urine was collected and observed for macrohematuria, tested for microhematuria and proteinuria with reagent strips (Siemens Multistix 10 SG), then analyzed for *S. haematobium* eggs, at the local health center laboratory on the same day of collection. Microscopy for visualization of schistosome eggs was performed by x100 mag. using a light compound microscope and stained with Lugol's iodine. A urine sample was counted positive for UGS on the presence of hematuria[3] or at least one terminal-spined ovum seen[49]. The number of ova reported where classified as ≥50 (high intensity) or < 50 (low intensity)[2]. Next, consenting eligible girls and women were examined by clinical colposcopy with photo-documentation, using a hand-held colposcope (EVA COLPO, Mobile ODT). The obtained images were cross-checked against the WHO FGS pocket atlas[5] to record key sequelae. These were then saved in a coded database for the internal validation through blinded evaluation of cervical images from photo-colposcopy by external team members, following the cross examination with the WHO Pocket atlas. A minimal clinical indication for FGS was determined upon the presence of sandy patches, abnormal blood vessels and/or sandy patches on homogenous yellow areas, in line with the WHO FGS pocket atlas coding[5] after cross verification by external specialists.

Statistical Analysis

All numerical data collected were first imputed into computer system using the Microsoft excel database and later imported into the R (version 4.0.2) software for statistical analyses. In univariate analysis, frequencies and proportions were reported for socio-demographic, syndromic and clinical variables. In bivariate analysis, Pearson's chi-squared tests were used to test the association between the socio-demographic, clinical and syndromic reproductive health related variables (which serve as independent variables), against the dependent variables FGS and UGS. To further highlight such dependence, univariate logistic regression analyses was used, with the results presented in the form of unadjusted odds ratios. To identify most relevant variables amongst the reproductive health related independent variables associated to each of UGS and FGS, multivariate logistic regressions analyses were used, with the results presented in the form of adjusted odds ratios (AOR), alongside 95% confidence intervals (CI) and *p*-values based on the Wald's Test. To fit the models, only factors significantly related to the outcomes at a 25% level of significance in the univariate models were included. Multicollinearity between independent variables in the initial multivariate models were evaluated using the `vif` function in the `car R` package and our knowledge on how the variables were measured. The step function in the `R` package `stats` was applied to the resulting multivariate models after correcting for multicollinearity to select the "best" fitting model. The global significance of variables in the final models were evaluated based on analysis of deviance tables using the `anova` function in the `stats R` package. In all, the level of significance was set at *p*-value <0.05.

Results

A. General participant characteristics

A total sample population of 304 females were enrolled. All **304 participants were assessed for UGS but not all participants were diagnosed with FGS. Participants were** aged from 5 to 69 years old (193 of reproductive age, >13 and <70, with mean±SD age of 28 ±12.7). Also, 88.16% of participants were dependent on, and lived within a proximity of ≤200m to the Mape lake (Island communities), and the remaining 11.82% came from Mainland communities, which were further from

the lake (>400m), having alternative water sources (wells and stand taps), and involved in farming alone without fishing activities. A prevalence of 63.8% (194/304) for UGS was recorded from egg prevalence or hematuria. Furthermore, 27.30% showed proteinuria, and a 51.0% prevalence (155/304) was recorded for hematuria (with 19 showing macrohematuria). Microhematuria sensitivity and specificity was calculated against egg positivity, with a specificity and sensitivity of 80.00% (95% CI: 73.58 – 86.42) and 73.83% (95% CI: 66.91 – 80.75) respectively. The Geometric Mean Egg (GME) count was 33.1 (Range: 2 – 1220) among which 36.2% had heavy (≥ 50 eggs/10ml of urine) infection while 63.8% had light (> 50 eggs/10ml of urine) infection. Macrohematuria was strongly related to egg density categories ($\chi 2 = 17.7$; $P < 0.001$), where cases of macrohematuria were directly related to heavy egg load (93.2%). More than half of the study population reporting not having received treatment with praziquantel in more than a year (see Table 1). Reported sexual and reproductive health syndromes included miscarriages (58.89%), lower abdominal pain (56.95%), lower back pain (44.59%), coital pain (45.98%), coital bleeding (37.93), vaginal itches (68%), abnormal vaginal discharge (42.6%) and menstrual irregularities (47.74%), all seen to be comparatively higher amongst participants, compared to stress incontinence (19.47) (see Table 1).

Table 1: General characteristics of all study participants (Sociodemographic, syndromic, clinical)

Variable	Category	Number of Women	Percentage
1. Demographic			
Age (groups)	<14	111	36.51
(n=304/304)*	[14-19]	62	20.39
	[20-35]	83	27.3
	36+	48	15.79
Menarche*(n=304/304*)*	Pre	98	32.24
	Post	206	67.76
Age at marriage	[13-14]	71	39.89
(n=178/193)*	[15-17]	88	49.44
	18+	19	10.67
No of Children	0	44	24.31
(n=181/193)*	[1-3]	72	39.78
	[4-6]	37	20.44
	7+	28	15.47
Age of last child	0+	10	7.69
(n=130/137)*	[1-3]	67	51.54
	[4-6]	15	11.54
	7+	38	29.23
Treatment with praziquantel	< 12 months	1	0.3
(n=304/304)*	> 12 months	292	96.1
	Never	11	3.6
Economic Activity	Fishing (with/without farming)	211	87.5
(n=241/304)*	Farming (without fishing)	30	12.4
Proximity to lake	<200m	268	88.16
(n=304/304)*	>400m	36	11.84

2. Syndromic			
Lower Abdominal Pain*(n=223/304*)*	Yes	127	56.95
Coital Pain*(n=174/193*)*	Yes	80	45.98
Coital bleeding*(n=174/193*)*	Yes	66	37.93
Vaginal Itches*(n=225/304*)*	Yes	153	68.00
Vaginal Discharge*(n=214/304*)*	Yes	90	42.06
External genital Itch*(n=206/304*)*	Yes	86	41.75
Lower back Pain*(n=223/304*)*	Yes	99	44.59
Stress Incontinence*(n=226/304*)*	Yes	44	19.47
Menstrual Irregularities*(n=199/206*)*	Yes	95	47.74
Miscarriages*(n=180/193*)*	0	74	41.11
	1+	106	58.89
3. Clinical			
Parasitemia*(n=304/304*)*	0	141	46.38
	[1-50]	104	34.21
	50+	59	19.41
Hematuria*(n=304/304*)*	+	155	51.0
Proteinuria*(n=304/304*)*	+	83	27.30

*Shows the eligible sample size for each variable. For age of marriage (*n=178/193**) for example, 178 out of the 193 eligible women gave information their marriage age, meaning 15 women had missing information for the variable.

1. UGS Characteristics amongst sample population

Table 2 presents the relationship between UGS as a dependent factor and each of the sociodemographic and reported reproductive health characteristics based on chi-square tests of independence and univariate logistic regression. The results indicate that the chances of UGS infection amongst women who lived more than 400m from the lake was 0.36 (95% CI: 0.17-0.72) times that of women who lived less than 200m to the lake, implying that significant odds of being infected with UGS was seen with closer lake proximity. A significant decrease in chances of infection with urogenital schistosomiasis was observed with increasing age. Relative to girls <14 years, girls between 14-19 years had a 0.46 (95% CI: 0.22-0.95) odds of having UGS, as opposed to 0.29 (95% CI: 0.15-0.54) odds for adults ranging from 20-35 years, and 0.09 (95% CI: 0.04-0.19) odds for women older than 35 years. All reported reproductive health syndromes showed significant relationship with UGS, except for stress incontinence (UOR 1.72 [95% CI: 0.87-3.54] p= 0.1287). In effect, women with lower abdominal pain, coital pain, vaginal itch, menstrual irregularity, and coital bleeding showed significantly higher odds (Table 2) of UGS.

Table 2: Relations between UGS and each socio-demographic and syndromic variable in the study sample

		Chi2 test of Independence	**Univariate logistic regression**

Variables	Category	N	UGS – n (%)	UGS + n (%)	P-value	Unadjusted OR (95% C.I.)			P value
Age group	<14	111	20 (18.2)	91 (46.9)		1			
	[14-19]	62	20 (18.2)	42 (21.6)		0.46	(0.22,	0.95)	0.0352
(n=304)	[20-35]	83	36 (32.7)	47 (24.2)		0.29	(0.15,	0.54)	0.0002
	36+	48	34 (30.9)	14 (7.2)	<0.0001	0.09	(0.04,	0.19)	<0.0001
No of Children	0	44	15 (18.1)	29 (29.6)		1			
(n=181)	[1-3]	72	33 (39.8)	39 (39.8)		0.61	(0.28,	1.32)	0.2143
	[4-6]	37	16 (19.3)	21 (21.4)		0.68	(0.27,	1.67)	0.3994
	7+	28	19 (22.9)	9 (9.2)	0.0462	0.25	(0.09,	0.66)	0.0063
Age of Last Child	0+	10	4 (6)	6 (9.5)		1			
(n=130)	[1-3]	67	33 (49.3)	34 (54)		0.69	(0.16,	2.62)	0.5863
	[4-6]	15	4 (6)	11 (17.5)		1.83	(0.33,	10.6)	0.4862
	7+	38	26 (38.8)	12 (19)	0.0323	0.31	(0.07,	1.27)	0.1082
Miscarriages	0	74	41 (48.8)	33 (34.4)		1			
(n=180)	1	52	19 (22.6)	33 (34.4)		2.16	(1.05,	4.52)	0.0382
	2+	54	24 (28.6)	30 (31.2)	0.1055	1.55	(0.77,	3.17)	0.2216
Lower Abdominal Pain*(n=223)*	Yes	127	42 (45.2)	85 (65.4)	0.0039	2.29	(1.33,	3.98)	0.0028
Coital Pain*(n=174)*	Yes	80	25 (30.5)	55 (59.8)	0.0001	3.39	(1.82,	6.43)	0.0001
Coital bleeding*(n=174)*	Yes	66	19 (23.2)	47 (51.1)	0.0002	3.46	(1.82,	6.79)	0.0002
Vaginal Itches*(n=225)*	Yes	153	51 (53.7)	102 (78.5)	0.0001	3.14	(1.77,	5.67)	0.0001
Abnormal Vaginal Discharge *(n=214)*	Yes	90	27 (29)	63 (52.1)	0.0008	2.66	(1.51,	4.76)	0.0008
Lower Back Pain*(n=222)*	Yes	99	34 (36.6)	65 (50.4)	0.0551	1.76	(1.03,	3.06)	0.0416
Stress Incontinence*(n=226)*	Yes	44	14 (14.7)	30 (22.9)	0.1729	1.72	(0.87,	3.54)	0.1287
Genital Itches*(n=206)*	Yes	86	26 (28.6)	60 (52.2)	0.0007	2.73	(1.53,	4.94)	0.0008
Menstrual Irregularity*(n=199)*	Yes	95	29 (33)	66 (59.5)	0.0002	2.98	(1.68,	5.4)	0.0002
Proximity to lake	<20m	268	89 (80.9)	179 (92.3)		1			
	>200m	36	21 (19.1)	15 (7.7)	0.0051	0.36	(0.17,	0.72)	0.0042

Multivariate Logistic Regression Model for Reporting Sexual and Reproductive Health (SRH) Risk Factors related to UGS

After including all variables significantly related to UGS at a 25% level in a multivariate model, multicollinearity issues were suspected between lower abdominal pain and lower back pain, and external genital itch and vaginal itches. However, considering genital itch responses were most often related to vaginal itch or misreported by respondents due to their literal similarity in Pidgin English or Fulbe used during questioning, we resorted to keeping only vaginal itches in the model. Similarly for lower back pain and lower abdominal pain because of the similarity in responses, but with a more comprehensive responding for lower abdominal pain, lower back pain was removed. The resulting "best" fitting model included age group, lower abdominal pain, and coital pain as the most significant sexual and reproductive health risk factors for UGS (Table 3). In this result, we also observed a decreasing trend in number of cases of UGS with increasing age. Also, the odds of infection in women with lower abdominal pain was 6.42 (95% CI: 2.85 - 15.68) times that for women without the pain. The odds of infection in women with coital pain was 2.16 (95% CI: 1.05 – 4.46) times that for women without the pain.

Table 3: Possible risk factors for UGS amongst the socio-demographic and SRH included in the study. A multivariate logistic regression model on the effects of sexual and reproductive health factors significantly related to UGS.

SRH Indicator	Category	Adjusted OR (95% C.I.)	P value
Age group	[14-19]	1.0	
	[20-35]	0.28 (0.10, 0.70)	0.0087
	36+	0.11 (0.04, 0.31)	0.0001
Lower Abdominal Pain	No	1.0	
	Yes	6.42 (2.85, 15.68)	0.0000
Coital Pain	No	1.0	
	Yes	2.16 (1.05, 4.46)	0.0362

2. FGS Characteristics amongst study participants (Sub-group)

Of the total number of participants examined for FGS after UGS (n=67), 40 were confirmed to have ova-patent UGS, and 34 for FGS, upon the presence of homogenous yellow sandy patches, grainy sandy patches, and abnormal blood vessels (Figure 2). A breakdown of UGS/FGS within the subset of 67 women examined for FGS showed: 26 FGS+/UGS+; 8 FGS+/UGS-; 14 FGS-/UGS+; and 19 FGS-/UGS-. Related reproductive health syndromes (as reported in UGS), similarly, were all found to have some association ($P < 0.05$) with FGS manifestation amongst females (Table 4), except for stress incontinence. Of import amongst these, menstrual irregularities or abnormality, also found with UGS, was seen to have 7.9 times higher odds of affecting women with FGS than women without FGS (Table 4). Back pain was seen to significantly affect women with FGS manifestations than was the case with UGS. Similarly, odds of having FGS manifestations were seen to ascend with age (Table 4), unlike UGS which was significant with descending age. Lower abdominal pain, menstrual irregularity and lower back pain showed the highest odds of manifesting amongst women with FGS.

Figure 2: Imagery of FGS pathology of the cervix with reported lesions (magnification x4)

A) 1-rubbery papule, 2-abnormal blood vessel, 3- homogeneous sandy patch (30-year-old woman, +UGS, +lower abdominal pain, +Menstrual irregularity); **B)** 1,2- grainy sandy patches (45-year-old woman, -UGS, +lower abdominal pain; +Menstrual irregularity)

Table 4: Relations between FGS and socio-demographic and syndromic variables in the sub-group of girls and women diagnosed for FGS

Variables*(n=67)*	Category	N	Chi2 Test of Independence			Univariate logistic regression			
			FGS – n(%)	FGS + n(%)	P-value	Unadjusted OR (95% C.I.)			P value
Age group	[14-19]	19	15 (45.5)	4 (11.8)		1			
	[20-35]	29	11 (33.3)	18 (52.9)		6.14	(1.73,	26.1)	0.0077
	36+	19	7 (21.2)	12 (35.3)	0.0091	6.43	(1.62,	30.35)	0.0116
Age at Marriage	[13-14]	23	10 (30.3)	13 (38.2)		1			
	[15-17]	38	22 (66.7)	16 (47.1)		0.56	(0.19,	1.58)	0.2765
	18+	6	1 (3)	5 (14.7)	0.1286	3.85	(0.51,	79.99)	0.2510
No of Children	0	16	12 (36.4)	4 (11.8)		1			
	[1-3]	22	12 (36.4)	10 (29.4)		2.5	(0.64,	11.23)	0.2024
	[4-6]	15	4 (12.1)	11 (32.4)		8.25	(1.79,	46.95)	0.0102
	7+	14	5 (15.2)	9 (26.5)	0.0363	5.4	(1.19,	28.98)	0.0357
Age of Last Child	0+	1	1 (4.8)	0 (0)		1			
	[1-3]	27	14 (66.7)	13 (46.4)		Inf	(0,	Inf)	0.9965
	[4-6]	4	0 (0)	4 (14.3)		Inf	(0,	Inf)	0.9937
	7+	17	6 (28.6)	11 (39.3)	0.1199	Inf	(0,	Inf)	0.9963
Miscarriages	0	26	18 (54.5)	8 (23.5)		1			
	1	22	8 (24.2)	14 (41.2)		3.94	(1.22,	13.78)	0.0256
	2+	19	7 (21.2)	12 (35.3)	0.0362	3.86	(1.14,	14.19)	0.0343
Lower Abdominal Pain	Yes	47	15 (45.5)	32 (94.1)	0	19.2	(4.74,	131.08)	0.0003
Coital Pain	Yes	32	10 (30.3)	22 (64.7)	0.0071	4.22	(1.55,	12.16)	0.0058
Coital bleeding	Yes	29	8 (24.2)	21 (61.8)	0.0029	5.05	(1.82,	15.19)	0.0026
Vaginal Itches	Yes	49	18 (54.5)	31 (91.2)	0.0009	8.61	(2.44,	40.95)	0.0021
Vaginal Discharge	Yes	32	9 (27.3)	23 (67.6)	0.0014	5.58	(2.01,	16.67)	0.0013
Back Pain	Yes	41	12 (36.4)	29 (85.3)	0	10.15	(3.31,	36.45)	0.0001
Stress Incontinence	Yes	10	0 (0)	10 (29.4)	0.0009	Inf	(0,	Inf)	0.9927
Genital Itch	Yes	32	9 (27.3)	23 (67.6)	0.0014	5.58	(2.01,	16.67)	0.0013
Menstrual irregularities	Yes	34	9 (27.3)	25 (73.5)	0.0002	7.41	(2.61,	23)	0.0003
Proximity	<20m	60	30 (90.9)	30 (88.2)	1	1			
	>200m	7	3 (9.1)	4 (11.8)	1	1.33	(0.27,	7.25)	0.7212

Multivariate Logistic Regression Model for Reporting Sexual and Reproductive Health (SRH) Risk Factors related to FGS

Similar to UGS, a multivariate model was constructed with all variables significantly related to FGS at a 25% level. As well, multicollinearity checks revealed lower back pain and genital itch (for same reasons) with the variables age group, coital pain, vaginal itches, and lower abdominal pain (Table 5) retained in the "best" fitting model.

Table 5: Possible risk factors amongst SRH for FGS. A multivariate logistic regression model on the effects of FGS on sexual and reproductive health factors.

SRH Indicator	Category	Adjusted OR (95% C.I.)	P value
Age group	[14-19]		
	[20-35]	20.15 (2.92, 240.94)	0.0061
	36+	41.29 (4.16, 946.69)	0.0054
Coital Pain	No	1.0	
	Yes	10.44 (2.12, 90.91)	0.0105
Vaginal Itches	No	1.0	
	Yes	12.50 (1.92, 128.77)	0.0151

Lower Abdominal Pain	No	1.0	
	Yes	28.80 (3.36, 578.24)	0.0081

3. UGS, FGS and associations with reproductive health characteristics

Age, number of children, age of last child, menstrual abnormality, miscarriages, and lower abdominal pain were identified as possible reproductive health factors associated with *S. haematobium* infection and were used within this study. Generally, both FGS and UGS were not significantly (*P*-value >0.05) related to number of children, age of last child and miscarriages. In multivariate logistic regression models, after selection of the best fitting models, the results show that the most significant risk factors for UGS are age group, lower abdominal pain and coital pain (Table 4), whereas age-group and lower abdominal pain, coital pain and vaginal itches were identified as the most significant risk factors for FGS (Table 5).Chances of FGS manifestations amongst women with lower abdominal pain was AOR 9.5(95% CI:1.7-81.8) times that of women without the pain (Table 5). Analysis of deviance tables for both best fitting models (FGS and UGS), with *p*-values based on likelihood ratio tests are reported in Supplementary File 2.

Discussion

Understanding the risks and associations of UGS and FGS, especially within different contexts of women's health[41, 50], sheds greater light on the disease epidemiology, which could foster improved and coordinated control measures both locally and nationally[41]. Furthermore, precisely documenting existing associations between both UGS and FGS could clarify further the need for precision mapping of schistosomiasis in endemic regions, for formulating a better targeted integrated response[48]. Though a non-significant association was observed between egg intensity in urine and FGS from the onset of this study (Table 2), parasitemia association has been shown to be misleading in UGS[7, 12, 13] from several other studies[13] and reports on FGS, particularly when only a single urine sample is examined which is usually the case for population-based surveillance[6]. Considering this, questionnaire (for symptoms)[10, 21], as well as visual examination of cervix and vaginal walls by colposcopy[12, 18,

51], offers an added strength to single sample urinalysis for detection of FGS, as carried out in this study, and several others[10, 18]. The possibility of the presence of FGS in UGS populations has been often raised[8, 21],with projections of about 360 million girls and women possibly having UGS[15], but today it is thought that at least 56 million adolescent girls and women are suffering from FGS[15, 17]. Our results seem to show an even higher rate of FGS amongst the UGS infected population with an approximate FGS/UGS ratio of 34/40. Our study, given our application of portable colposcopy, is the first formal attempt to document the pathology of FGS in a primary care setting in Cameroon.

Elsewhere, the clinical pathology of FGS has been described resulting from the complex inflammatory responses to antigens released by adult worms and viable eggs[6, 14], which persists until sometime after adult worms are stopped egg-laying or are destroyed by praziquantel[24]. Thereafter, various signs and symptoms (or effects) may present months or even years after treatment[23, 42].

From present results, and within the general literature[15, 17], one of such effects noted is an effect on menstrual health. More than half of women within the study who reported poor menstrual health (FGS = 73.5%; UGS = 54.6%), either as irregular, painful or seized menstruation, were found to either shed eggs in urine (positive for UGS), or were positive for FGS, but without eggs in urine; showing more women positive for FGS reporting abnormal menstruation, than for UGS. This confirms recent analysis[17, 33] and suggests strong linkages between menstrual health management and FGS[15, 17], an under researched area. This can be credited to the fact that symptoms perhaps diminished after a while with UGS (maybe as a result of treatment in mass drug administration campaigns), but later resurface with more chronic sequelae of FGS[17], and with more dire symptoms and negative impact on menstrual health[17, 33]. In our study context, post-menarche females already faced a substantial challenge with limited access to hygienic material and information on menstrual health management, typically relying on self-made clothes and absorbent plant leaves during menstruation, due to lack of finances or general knowledge.

Still related to FGS and menstrual health, narratives from a previous study[33] which used qualitative probing showed women having manifestations of FGS and not shedding eggs in urine, gave a history of having lived in their earlier years in heavily infested *S. haematobium* foci. This explained their later

manifestation of FGS symptoms, even after having moved away to a less infested area, with more than 90% limit in fresh water contact[33]. This is similar to our findings, where lake proximity was seen to be not very significant to FGS manifestation (Table 4), same as egg shedding, still pointing to early-in-life infection and later chronicity. Significant difference in menstrual abnormalities amongst UGS positive women [n=22 (56.4%)] and UGS negative women [n=12 (44.4%)], alerts to future chronicity of FGS after UGS, especially if not managed with more readily available praziquantel treatment(s)[42, 52].

On its own, lower abdominal pain observed significant association (in adjusted and unadjusted regression models) in both UGS and FGS. The chances of having lower abdominal pain were significantly higher in females with either FGS (94.1%) or UGS (84.2%). Similarly with coital pain and vaginal itches, these reported as key indicators for UGS and FGS, directing early diagnosis of UGS and future FGS in endemic communities, thereby promoting the verticalization of control strategies for both diseases.

Another trend observed in this study is that intensity of infection or egg patent-prevalence (for UGS) reduces while chronic disease or morbidity for FGS increases as women age. The chances of FGS after UGS increased significantly (AOR 6.43,95% C.I 1.62-30.35, P=0.0091) as women aged (36+). Similar findings have been reported in other studies in different geographical locations[6, 14, 53, 54] and recently in this area[33]; emphasizing on the level of present intensity for UGS, and possible future occurrence of FGS[14, 54]. UGS at a younger age will in some cases manifest into FGS when the female is older[14], causing more intense gynecological symptoms and effects. This offers a possible guiding tool for better control policies, related to early diagnosis and treatment[41, 55]. This surpasses need alone for school-based MDAs[13, 28, 56], but considers and encourages individual therapy in different contexts for FGS (and MGS)[6].

Although only a few amongst the extensive list of reproductive health determinants [54] were identified in this study to be statistically significant, where mostly reported symptoms were collected, clinical and biological examinations carried out, enabled confirmation of how future self-reported symptoms with UGS and FGS might be best used[33]. These results support the advocated need for further attention on

post-transmission schistosomiasis[57], and also, the availability of praziquantel in lowest level (Health Areas and community) health care for individual therapy[54], as well as treatment from a younger age[15, 28, 41, 52], buoyed with the recent development of pediatric praziquantel[58].

Study Limitations

Though described as gold standard[49], active UGS was only detected through observation of eggs in urine samples by microscopic-based poly-carbonate filter examination, as well as recommended dipstick assays for urinary hematuria detection. Alternative molecular assays such as polymerase chain reaction (PCR) for schistosome detection in human serum and urine samples[12], were not considered for added sensitivity for UGS and FGS (in vaginal lavage analysis)[3, 59]. Though recommended[12, 21], only visual examination through inspection for lesions on the cervix, the fornices, and the vaginal walls with a colposcope[5, 51] and screening with questionnaires[10] was considered in the detection of FGS in this study. Lastly, clinical diagnosis of FGS was carried out only on a limited sub-group of females, where more precise conclusions may be obtained by using an appropriate sample size.

Conclusion

Whilst millions of women in Cameroon have UGS, its epidemiological connection with FGS is not fully appreciated, which creates an unfortunate knowledge holdup for effective control at the public health level. In our chosen study location, which is broadly typical for endemic areas of UGS in Cameroon[21, 34, 36, 40], strong epidemiological associations between UGS and FGS were found against certain key sexual and reproductive determinants: age, lower abdominal pain and menstrual health. This formative knowledge could be utilized to tackle and ultimately prevent FGS, with a more targeted integrated control for UGS in Cameroon and elsewhere in endemics areas for UGS globally. This study further adds detailed insight into the connection of FGS and UGS within primary care in endemic communities, denoting those with cardinal symptomologies more explicitly for scalable detection and targeted control of FGS within UGS endemic areas.

Supporting Files

Supplementary File 1.docx : Structured questionnaire

Supplementary File 2.docx: Deviance Table

Declarations

- **Authors' contributions**

MCM and JRS conceptualized the study and planned the methodology; AEN,VG, MCM, carried out field investigation; FNB, MCM, JRS, ASO, AEN, VG, analyzed and interpreted the data for this manuscript; MCM acquired funding for study and wrote the original draft of the manuscript; JRS supervised the study and was a major contributor in the conceptualization and writing of the manuscript; AEN, coordinated field activities within the Malantouen Health District; AEN, FNB, VG, ASO, reviewed and edited the manuscript. All authors approved the final version of the paper before submission**.**

- **Competing interests**

The authors declare that they have no competing interests.

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- **Data Sharing Statement**

All data generated or analysed during this study are included in this published article [and its supplementary files].

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- **License Statement**

- **Consent for publication**

Written informed consent for publication of clinical details and/or clinical images was obtained from the patients and parents/guardians where needed.

References

1. Freer JB, Bourke CD, Durhuus GH, Kjetland EF, Prendergast AJ. Schistosomiasis in the first 1000 days. The Lancet Infectious Diseases. 2018;18(6):e193-e203.
2. WHO. Prevention and Control of Schistosomiasis and Soil Transmitted Helminths Geneva: WHO; 2002 [33/63]. Available from: http://apps.who.int/iris/bitstream/handle/10665/42588/WHO_TRS_912.pdf;jsessionid=297C20DDFCBFFF9F9AAE9DF120C0F834?sequence=1.
3. Utzinger J, Becker SL, van Lieshout L, van Dam GJ, Knopp S. New diagnostic tools in schistosomiasis. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2015;21(6):529-42.
4. Søfteland S, Sebitloane MH, Taylor M, Roald BB, Holmen S, Galappaththi-Arachchige HN, et al. A systematic review of handheld tools in lieu of colposcopy for cervical neoplasia and female genital schistosomiasis. International Journal of Gynecology & Obstetrics. 2021;153(2):190-9.
5. WHO. Female Genital Schistosomiasis: A Pocket Atlas for Clinical Health-Care Professionals Geneva: WHO Press; 2015 [Available from: https://www.who.int/publications/i/item/9789241509299.
6. Kjetland E, Leutscher P, Ndhlovu P. A review of female genital schistosomiasis. Trends in Parasitology. 2012;28(2):58-65.
7. Poggensee G, Kiwelu I, Saria M, Richter J, Krantz I, Feldmeier H. Schistosomiasis of the lower reproductive tract without egg excretion in urine. The American journal of tropical medicine and hygiene. 1998;59(5):782-3.
8. Christinet V, Lazdins-Helds J, Stothard J, Reinhard-Rupp J. Female genital schistosomiasis (FGS): from case reports to a call for concerted action against this neglected gynaecological disease. International Journal for Parasitology. 2016;46(7):395-404.
9. Shams M, Khazaei S, Ghasemi E, Nazari N, Javanmardi E, Majidiani H, et al. Prevalence of urinary schistosomiasis in women: a systematic review and meta-analysis of recently published literature (2016–2020). Tropical Medicine and Health. 2022;50(1):12.
10. Ekpo U, Odeyemi O, Sam-Wobo S, Onunkwor O, Mogaji H, Oluwole A, et al. Female genital schistosomiasis (FGS) in Ogun State, Nigeria: a pilot survey on genital symptoms and clinical findings. Parasitology Open. 2017;3:e10.
11. Hotez PJ, Engels D, Gyapong M, Ducker C, Malecela MN. Female Genital Schistosomiasis. New England Journal of Medicine. 2019;381(26):2493-5.
12. Galappaththi-Arachchige HN, Holmen S, Koukounari A, Kleppa E, Pillay P, Sebitloane M, et al. Evaluating diagnostic indicators of urogenital Schistosoma haematobium infection in young women: A cross sectional study in rural South Africa. PloS one. 2018;13(2):e0191459.
13. Wiegand RE, Fleming FM, de Vlas SJ, Odiere MR, Kinung'hi S, King CH, et al. Defining elimination as a public health problem for schistosomiasis control programmes: beyond prevalence of heavy-intensity infections. The Lancet Global Health. 2022;10(9):e1355-e9.
14. Hegertun I, Gundersen S, Kleppa E, Zulu S, Gundersen S, Taylor M, et al. S. haematobium as a common cause of genital morbidity in girls: a cross-sectional study of children in South Africa. PLoS neglected tropical diseases. 2013;7(3):e2104.

15. UNAIDS. 'No more neglect:Female genital schistosomiasis and HIV. www.unaids.org/en/resources/documents/2019/: UNAIDS; 2019.
16. Hotez P. Speaking of Medicine and Health [Internet]. BLOGS P, editor: PLOS BLOGS. 2013. Available from: https://speakingofmedicine.plos.org/2013/05/06/female-genital-schistosomiasis-fgs-sub-saharan-africas-secret-scourge-of-girls-and-women/.
17. Stothard JR, Odiere MR, Phillips-Howard PA. Connecting Female Genital Schistosomiasis and Menstrual Hygiene Initiatives. Trends in Parasitology. 2020;38(5).
18. Bustinduy AL, Randriansolo B, Sturt AS, Kayuni SA, Leustcher PDC, Webster BL, et al. An update on female and male genital schistosomiasis and a call to integrate efforts to escalate diagnosis, treatment and awareness in endemic and non-endemic settings: The time is now. In: Rollinson D, Stothard R, editors. Advances in Parasitology. 115: Academic Press; 2022. p. 1-44.
19. Majangara Karaga R. Concealed urogenital schistosomiasis causing chronic pelvic pain: A case report. Clinical Case Reports. 2021;9(4):1860-4.
20. Stothard J. Female genital schistosomiasis - icebergs of morbidity ahead? Trends in parasitology. 2012;28(5):174-5.
21. Campbell S, Stothard J, O'Halloran F, Sankey D, Durant T, Ombede D, et al. Urogenital schistosomiasis and soil-transmitted helminthiasis (STH) in Cameroon: An epidemiological update at Barombi Mbo and Barombi Kotto crater lakes assessing prospects for intensified control interventions. Infectious diseases of poverty. 2017;6(1):49-.
22. King C. Parasites and poverty: the case of schistosomiasis. Acta tropica. 2010;113(2):95-104.
23. Kjetland EF, Mduluza T, Ndhlovu PD, Gomo E, Gwanzura L, Midzi N, et al. Genital schistosomiasis in women: a clinical 12-month in vivo study following treatment with praziquantel. Trans R Soc Trop Med Hyg. 2006;100(8):740-52.
24. Treatment of Female Genital Schistosomiasis (FGS) With Praziquantel: A Proof-of-Concept Study (NCT04115072) [Internet]. NIH: ClinicalTrials.gov archive. 2020 [cited 31/01/2022].
25. Brindley PJ, Hotez PJ. Break Out: urogenital schistosomiasis and Schistosoma haematobium infection in the post-genomic era. PLoS Negl Trop Dis. 2013;7(3):e1961.
26. Secor WE, Colley DG. When Should the Emphasis on Schistosomiasis Control Move to Elimination? Trop Med Infect Dis. 2018;3(3).
27. Kukula VA, MacPherson EE, Tsey IH, Stothard JR, Theobald S, Gyapong M. A major hurdle in the elimination of urogenital schistosomiasis revealed: Identifying key gaps in knowledge and understanding of female genital schistosomiasis within communities and local health workers. PLoS neglected tropical diseases. 2019;13(3):e0007207.
28. Faust CL, Osakunor DNM, Downs JA, Kayuni S, Stothard JR, Lamberton PHL, et al. Schistosomiasis Control: Leave No Age Group Behind. Trends Parasitol. 2020;36(7):582-91.
29. World Health Organisation. WHO guideline on control and elimination of human schistosomiasis. https://www.who.int/publications/i/item/9789240041608: WHO; 2022. p. 142.
30. Bergquist R, Yang G-J, Knopp S, Utzinger J, Tanner M. Surveillance and response: Tools and approaches for the elimination stage of neglected tropical diseases. Acta Tropica. 2015;141:229-34.
31. SCI Foundation. FAST PACKAGE PROJECT 2021 [Available from: https://schistosomiasiscontrolinitiative.org/projects/fast-research-project
32. Ndassi VD, Anchang-Kimbi JK, Sumbele IUN, Ngufor LA, Nadege K, Kimbi HK. The epidemiological status of urogenital schistosomiasis among reproductive aged individuals in the Tiko Health Area- a semi-urban setting in the Mount Cameroon area. PLOS Neglected Tropical Diseases. 2021;15(1):e0008978.
33. Masong MC, Wepnje GB, Marlene NT, Gamba V, Mengue M-T, Kouokam E, et al. Female Genital Schistosomiasis (FGS) in Cameroon: A formative epidemiological and socioeconomic investigation in eleven rural fishing communities. PLOS Global Public Health. 2021;1(10):e0000007.
34. TchuentÉ LAT, N'Goran EK. Schistosomiasis and soil-transmitted helminthiasis control in Cameroon and Côte d'Ivoire: implementing control on a limited budget. Parasitology. 2009;136(13):1739-45.

35. National Program for the control of Schistosomiaisis and intestinal helminthiases MoPHC. Towards elimination of Schistosomiasis and Soil-transmitted Helminthiasis and in Cameroon: A road map for paradigm shift 2021-2030. MINSANTE, Yaoundé: MINSANTE; 2022.
36. National Program for the control of Schistosomiaisis and intestinal helminthiases. Progress Report Cameroon 2013-2019. Yaoundé: MINSANTE; 2019.
37. World Health Organization. Global update on implementation of preventive chemotherapy against neglected tropical diseases in 2018. Weekly Epidemiological Record 2019;94(38):425-38.
38. Crompton DWT, World Health Organization. Preventive chemotherapy in human helminthiasis : coordinated use of anthelminthic drugs in control interventions : a manual for health professionals and programme managers. Geneva: World Health Organization; 2006.
39. Makia C, Ozano K, Tagne M, Tchoffo M, Ngang S, Thomson R, et al. Achieving equity in UHC interventions: who is left behind by neglected tropical disease programmes in Cameroon? Glob Health Action. 2021;14(1):1886457-.
40. Njunda A, Ndzi E, Assob J, Kamga H, Kwenti E. Prevalence and factors associated with urogenital schistosomiasis among primary school children in barrage, Magba sub-division of Cameroon. BMC Public Health. 2017;17(1):618.
41. Deworming adolescent girls and women of reproductive age. Policy Brief [press release]. Geneva: WHO2022.
42. Nour M. Schistosomiasis: health effects on women. Rev Obstet Gynecol. 2010;3(1):28-32.
43. MINSANTE. Schistosomiasis distribution in Malanteoun Health District NTDmaps.org: MINSANTE; 2018 [Available from: https://ntdmaps.org/.
44. National Institute of Statistics Cameroon. Socio-economic statistics of Cameroon, 2015 Cameroon2004-2014 [Available from: https://cameroon.opendataforafrica.org/SESC2015/socio-economic-statistics-of-cameroon-2015.
45. Keptcheu T, Khan P, Gustave L, Gangue T. Some Haematological Parameters among Urinary Schistosomiasis-Malaria Coinfected Children in Suburb of Malentouen Health District, West Region Cameroon. International Journal of Tropical Disease & Health. 2020:34-44.
46. Daniels W. Biostastistics: A foundation for analysis in the health sciences. New York: Wiley & sons; 1999.
47. Gnoth C, Godehardt E, Frank-Herrmann P, et al. Definition and prevalence of subfertility and infertility. Human Reproduction (Oxford, England). 2005 May;20(5):1144-1147. DOI: 10.1093/humrep/deh870. PMID: 15802321.
48. Colley DG, Bustinduy AL, Secor WE, King CH. Human schistosomiasis. Lancet (London, England). 2014;383(9936):2253-64.
49. World Health Organisation. Schistosomiasis WHO: WHO; 2022 [cited 2022. Available from: https://www.who.int/news-room/fact-sheets/detail/schistosomiasis.
50. World Health Oganization. Regional Office for the Western Pacific. People Centered Health care: A policy framework. 2007.
51. Kjetland EF, Norseth HM, Taylor M, Lillebø K, Kleppa E, Holmen SD, et al. Classification of the lesions observed in female genital schistosomiasis. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2014;127(3):227-8.
52. Bustinduy AL, Friedman JF, Kjetland EF, Ezeamama AE, Kabatereine NB, Stothard JR, et al. Expanding Praziquantel (PZQ) Access beyond Mass Drug Administration Programs: Paving a Way Forward for a Pediatric PZQ Formulation for Schistosomiasis. PLOS Neglected Tropical Diseases. 2016;10(9):e0004946.
53. Chetty A, Omondi MA, Butters C, Smith KA, Katawa G, Ritter M, et al. Impact of Helminth Infections on Female Reproductive Health and Associated Diseases. Front Immunol. 2020;11:577516.
54. Stothard JR, Stanton, M, Bustinduy, A, Sousa-Figueiredo, J C, Van Dam, GT, Betson, M, et al.,. Diagnostics for schistosomiasis in Africa and Arabia: A review of present options in control and future needs for elimination. Camnbridge core. 2014(141):1947-61.

55. Richardson ST, Franklin AL, Rome ES, Simms-Cendan JS. Global Health: Urogenital Schistosomiasis in the Adolescent Girl. Journal of Pediatric and Adolescent Gynecology. 2016;29(4):326-32.
56. Oluwole AS, Ekpo UF, Nebe OJ, Akpan NM, Jacob SM, Amazigo UV, et al. The new WHO guideline for control and elimination of human schistosomiasis: implications for the Schistosomiasis Elimination Programme in Nigeria. Infectious Diseases of Poverty. 2022;11(1):111.
57. Giboda M, Bergquist R. Schistosomiasis at the Crossroad to Elimination: Review of Eclipsed Research with Emphasis on the Post-Transmission Agenda. 2022;7(4).
58. Pediatric Praziquantel Consortuim. Contract manufacturing agreement signed for production of new pediatric treatment for schistosomiasis 2021 [Available from: http//:https://www.pediatricpraziquantelconsortium.org/.
59. Sturt A, Webb E, Phiri C, Mweene T, Chola N, van Dam G, et al. Genital self-sampling compared with cervicovaginal lavage for the diagnosis of female genital schistosomiasis in Zambian women: The BILHIV study. PLOS Neglected Tropical Diseases. 2020;14(7):e0008337.

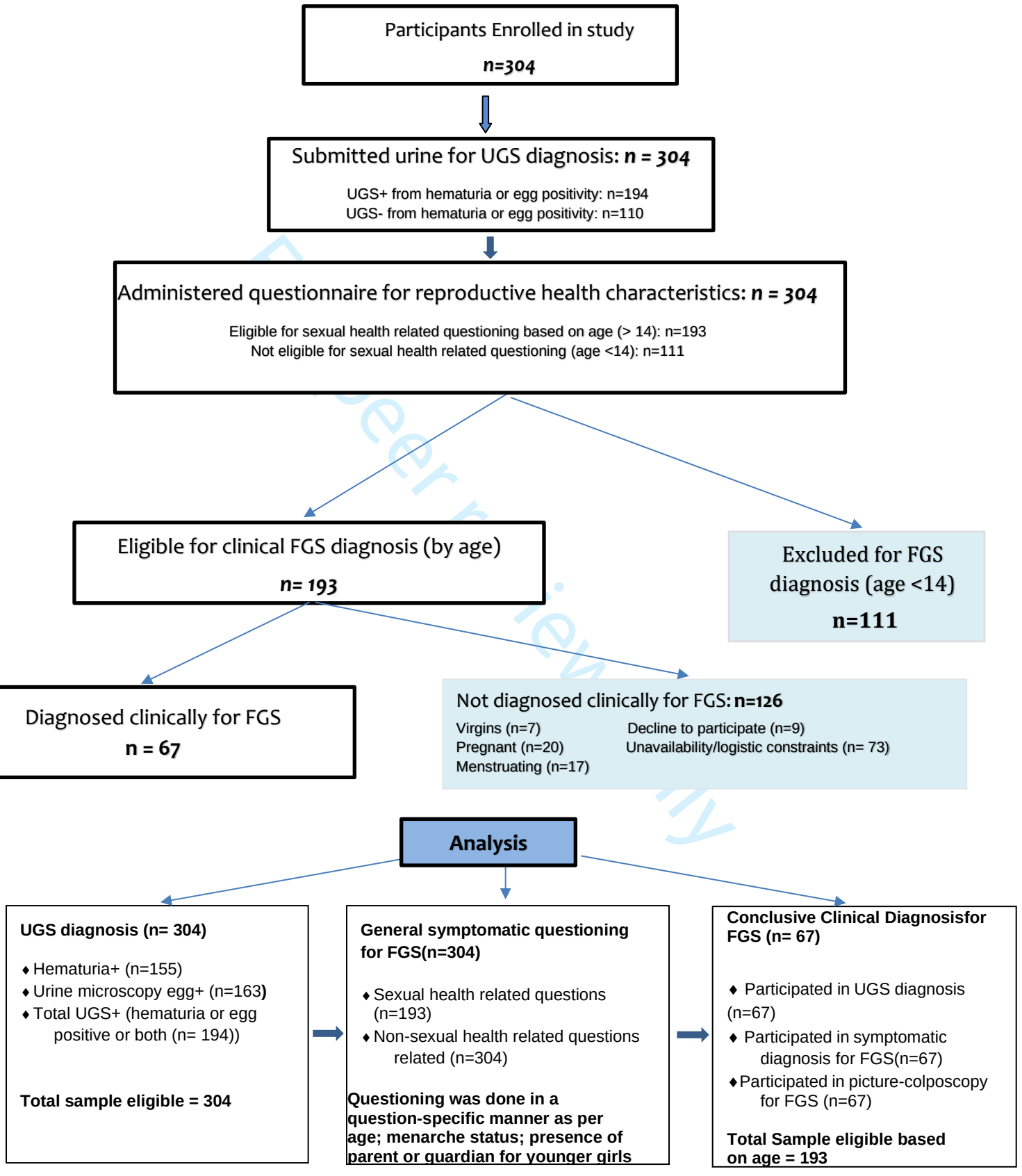
- **Figure Legends**

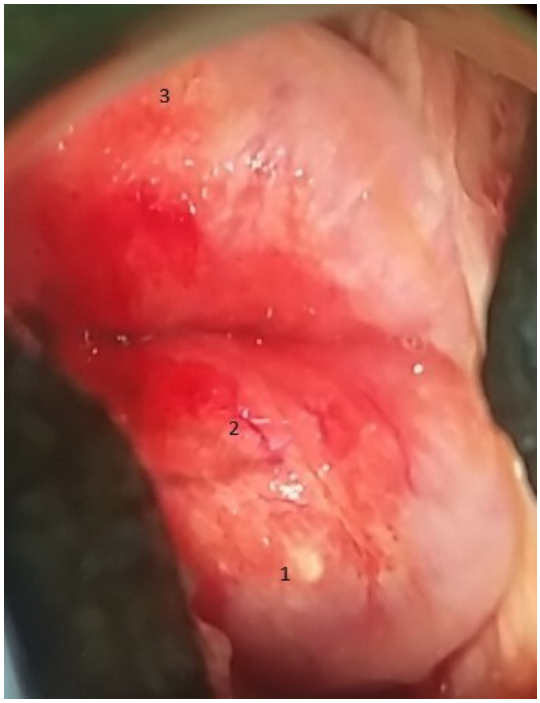
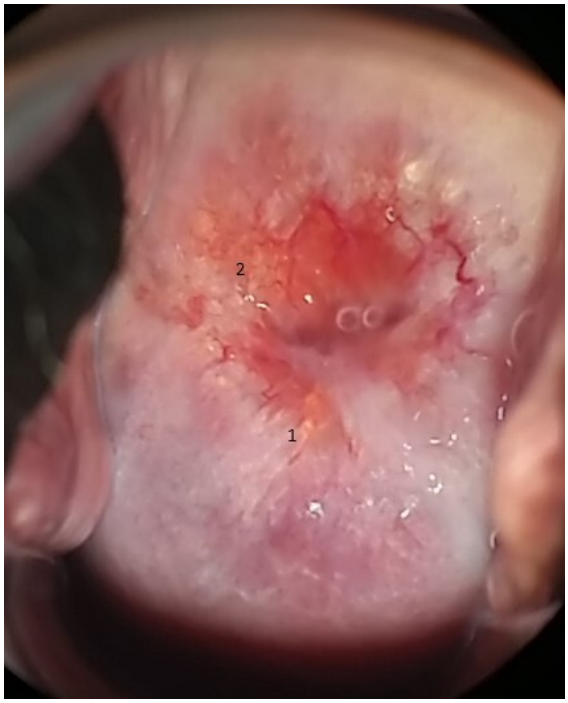
Figure1: Study participant selection criteria and numbers with diagnostic methods flow

Figure 2: Imagery of FGS pathology of the cervix with reported lesions (magnification of x4)

A) 1-rubbery papule, 2-abnormal blood vessel, 3- homogeneous sandy patch (30-year-old woman, +UGS, +lower abdominal pain, +Menstrual irregularity); **B**) 1,2- grainy sandy patches (45-year-old woman, -UGS, +lower abdominal pain; +Menstrual irregularity)

Sampling Flow Diagram



A	B
	

Supplemantary File 1

Close-ended structured questionnaire

A. Close ended structured questionnaire– Administered directly in English with oral translations into Fulbe, Kotoko, Mosgum, and Arab

Name of Community: _____

Age (years): _____

Education: Informal education () Formal education () (specify)_____

Marital Status: Single ( ) Married ( ) Separated ( ) Widowed ( )

No of years having lived in community _____

Previous community _____

Economic activity----------

Residence ---------- (collect coordinates)

Questions on symptoms of urinary tract schistosomiasis; FGS; OR STI

1. Do you see your menses? Yes ( ) No ( )
2. Did you observe/experience your menses within the last two weeks? Yes ( ) No ( ) Does your menses come every month? Regular?
3. Is your menses painful? _____(pain during menstruation – always very painful, sometimes painful, normal) Irregular? _____(every month?, not every month, stopped)
4. Do you have pain in your lower abdomen? When? For how long?
5. Do you have pain when urinating? Yes ( ) No ( )
6. Do you have difficulty in urinating (urine not coming out fluently)? Yes ( ) No ( )
7. Do you have sudden uncontrollable and unexpected urge to urinate and mostly cannot hold it? Even when you cough it comes out? Yes ( ) No ( )
8. Do you see blood in your urine? Yes () No ()
9. (If yes) When did you lastly see blood in your urine? _____Always, sometimes, Once in a while
10. Do you sometimes haveitching in your private part?Yes ( ) No ( )
11. How often do you experience this? Once a while ( ) frequently ( )/ When was the last time?
12. Do you have a feeling of burning within your private part? Yes ( ) No ( )

13. How often do you experience this? Once a while ( ) Frequently ( )

14. Do you sense a swelling/lumps within your private part? Yes ( ) No ( ) No response ( )

15. Do you have any discharge that comes from your vagina? Yes () No () Does it have an ordure? _____ Do you see the colour? Yes ( ) No ( ) What Color is it?White; grey; green/yellow; brown

16. Do you think this is normal? Yes () No() Do not know(). When did you start observing the discharge? Date _____

17. After sexual intercourse do you have a discharge? Yes () No () Is it smelly? Yes () No () Do not know ()

18. After or during sexual intercourse do you have pain?Yes ( ) No ( ) I do not know ( ) ; Do you have a bloody discharge?Yes ( ) No ( ) I do not know ( )

19. Have you had any miscarriages /pregnancies that passed? Yes ( ) No ( )

20. How many? ()

21. Do you have children? Yes() No()

22. What age is your last child? ()

23. Have you visited the clinic to complain about these issues? Yes ( ) No ( )

24. What you used/taken/done to treat any of these problems? _____ (Underline) Hospital or drug store/ local midwife/ traditional medicine/ prayers/ none of the above (what other? Specify)/nothing

Water contact History

1. Where do you fetch your household water? Lake; other source (name) _____
2. Do you fish in the lake? Yes (), No ()
3. Do you bathe in the lake? Yes (), No ()
4. What do you use the lake for? ()_____

Supplementary file 2

Analysis of deviance tables for both best fitting models (FGS and UGS), with *p*-values based on likelihood ratio tests

Variable	Df	Deviance	Resid. Df	Resid. Dev	Pr(>Chi)
UGS					
Age2	2	19.0094	162	208.70	7.450e-05 ***
Lower Abdominal Pain	1	25.6949	161	183.01	3.999e-07 ***
Coital Pain	1	4.4254	160	178.58	0.03541 *
FGS					
Age2	2	9.8057	64	83.061	0.0074253 **
Coital Pain	1	11.3146	63	71.747	0.0007690 ***
Vaginal Itches	1	13.1740	62	58.573	0.0002839 ***
Lower Abdominal Pain	1	10.5961	61	47.976	0.0011333 **

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-6
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	7-10
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	8-9
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	/
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*8-11*
Bias	9	Describe any efforts to address potential sources of bias	/
Study size	10	Explain how the study size was arrived at	7-9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9-10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	7-8
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	/

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	/
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11-13
		(b) Give reasons for non-participation at each stage	7-8
		(c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11-13
		(b) Indicate number of participants with missing data for each variable of interest	/
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	/
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	/
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	/
		Cross-sectional study—Report numbers of outcome events or summary measures	11-13
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9, 12-15
		(*b*) Report category boundaries when continuous variables were categorized	9, 12-15
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	/
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	/
Discussion			
Key results	18	Summarise key results with reference to study objectives	18-20
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	21
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.